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Theta Phase Synchrony Is Sensitive to Corollary Discharge Abnormalities in Early Illness Schizophrenia but Not in the Psychosis Risk Syndrome

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Background: **Prior studies have shown that the auditory N1 event-related potential component elicited by self-generated vocalizations is reduced relative to played back vocalizations, putatively reflecting a corollary discharge mechanism. Schizophrenia patients and psychosis risk syndrome (PRS) youth show deficient N1 suppression during vocalization, consistent with corollary discharge dysfunction. Because N1 is an admixture of theta (4–7 Hz) power and phase synchrony, we examined their contributions to N1 suppression during vocalization, as well as their sensitivity, relative to N1, to corollary discharge dysfunction in schizophrenia and PRS individuals.*** ***Methods.*** **Theta phase and power values were extracted from electroencephalography data acquired from PRS youth (n = 71), early illness schizophrenia patients (ESZ; n = 84), and healthy controls (HCs; n = 103) as they said "ah" (Talk) and then listened to the playback of their vocalizations (Listen). A principal component analysis extracted theta intertrial coherence (ITC; phase consistency) and event-related spectral power, peaking in the N1 latency range. Talk–Listen suppression scores were analyzed.*** ***Results:*** **Talk–Listen suppression was greater for theta ITC (Cohen's d = 1.46) than for N1 in HC (d = 0.63). Both were deficient in ESZ, but only N1 suppression was deficient in PRS. When deprived of variance shared with theta ITC suppression, N1 suppression no longer differentiated ESZ and PRS individuals from HC. Deficits in theta ITC suppression were correlated with delusions (P = .007) in ESZ. Theta power suppression did not differentiate groups.*** ***Conclusions.*** **Theta ITC-suppression during vocalization is a more sensitive index of corollary discharge-mediated auditory cortical suppression than N1 suppression and is more sensitive to corollary discharge dysfunction in ESZ than in PRS individuals.**

Key words: oscillations/N1/delusions/phase resetting/power/psychosis risk syndrome

Across the animal kingdom, the efference copy/corollary discharge mechanism allows all species to distinguish between self-generated sensations and those from external sources.[1–3] The general motif for this mechanism is thought to involve the transmission of an "efference copy" of motor commands to sensory regions, a corollary discharge signal representing the predicted sensory consequences of the impending motor act, and comparison of this prediction with the actual sensory consequences of the executed act, with matches typically leading to sensory suppression.[4] This mechanism both tags sensations as coming from "self" and minimizes the resources needed to process self-generated sensations. Vocalization studies in nonhuman primates show that auditory cortical responses are relatively inhibited during self-generated vocalizing and excited during passive listening,[5–7] putatively reflecting the operation of this mechanism.

In humans vocalizing, the corollary discharge mechanism during vocalization is studied with the electroencephalography (EEG) based N1 (or N100) event-related potential (ERP), generated in primary and secondary auditory cortex and peaking at about 100 ms poststimulus onset.[8] N1 to spoken sounds is relatively inhibited during vocalization compared to passive listening.[9–24] We and others have suggested that this is a "neural cost-effective" way of processing those sensations because less energy is needed to process predicted than unpredicted sensations.[25,26]

Importantly, this effect is disrupted in schizophrenia,[9–12,27,28] bipolar disorder,[12] schizotypy,[29] and in youth meeting criteria for the psychosis risk syndrome (PRS).[30] In first-degree relatives of schizophrenia and psychotic bipolar disorder patients, suppression values are intermediate between healthy controls (HCs) and ill probands.[12] While these findings suggest that deficient N1 suppression during vocalization is a marker of psychosis

vulnerability, it has generally not been associated with specific psychotic symptoms in prior studies.

ERPs recorded at the scalp are evidence of underlying synchronous activity among large assemblies of neurons firing at the same frequency in response to a stimulus or other event in a coordinated and consistent fashion across trials.[31] Specifically, after averaging together many EEG epochs time-locked to a sound, N1 emerges ~100 ms after sound onset. Traditionally, N1 was assumed to reflect neural activity uncorrelated with ongoing EEG activity, emerging only after reducing background EEG ("noise") through averaging. However, this assumption has been challenged by data showing that ERP components can also reflect an uncertain admixture of event-related synchronization (or phase resetting) of ongoing EEG oscillations and event-related change in the magnitude (ie, power) of oscillations. Thus, N1 elicited by a sound may reflect a combination of perturbations of ongoing oscillation phase and power plus a real neural response to the sound unrelated to the ongoing oscillations.[32–34]

Using time-frequency (TF) decomposition, event-related measures of power and phase resetting can be extracted from the ongoing EEG oscillations.[35] Total power is instantiated as an event-related spectral perturbation of EEG power compared to prestimulus levels. It most likely reflects both ERP signal power and trial-to-trial variability in power irrespective of whether the oscillations exhibit phase consistency.[36] Phase resetting is instantiated as phase synchronization of neural oscillations across trials, reflecting consistency in the phase of stimulus-evoked oscillations. Examining both single-trial power and intertrial phase coherence (ITC) may help better characterize event-related oscillatory brain dynamics[37] relative to traditional ERPs.

To understand the dynamics underlying N1 suppression during vocalization, we focus on the theta band because: N1 predominantly consists of activity in the theta band (4–8 Hz); theta band activity may play a critical role in long-range communication between motor and sensory areas during vocalization[14,38]; theta band synchrony may be involved in sensorimotor integration and provide voluntary motor systems with continually updated feedback on performance[39]; and somatostatin interneuron activity oscillates at a theta rhythm to recurrently inhibit excitatory pyramidal neurons.[40]

In this paper, we ask if theta total power and ITC are suppressed during talking compared to listening, like N1 is, and emerge as assays of corollary discharge-mediated auditory cortical suppression. We also ask about their sensitivity, relative to N1 suppression, in distinguishing HCs from patients with schizophrenia and the psychosis risk syndrome. Finally, we ask if abnormalities in theta total power and ITC assays of corollary discharge are related to the severity of positive symptoms as suggested by Feinberg[41] and others.[42] We expected that greater positive symptom ratings would negatively correlate with theta suppression measures such that greater symptom severity would be associated with less (ie, more abnormal) suppression. To this end, we conducted TF analyses of data previously published in the time-voltage domain as ERPs.[30]

Methods

Participants

Study participants included 71 individuals meeting psychosis risk syndrome (PRS) criteria based on the Structured Interview for Psychosis Risk Syndromes (SIPS),[43–45] 84 early illness DSM-IV schizophrenia patients (ESZ) based on the Structured Clinical Interview for DSM-IV (SCID),[46] and 103 healthy comparison (HC) subjects. Details appear in supplementary table S1).

Clinical Ratings

A trained research assistant, psychiatrist, or clinical psychologist rated symptoms in ESZ using the Scale for the Assessment of Positive Symptoms (SAPS).[47] Symptom rating interviews were typically done within 1 week of EEG recording, ranging from 64 days to the same day (mean = 8.1, SD = 8.7 days). Severity of PRS symptoms were rated using the Scale of Psychosis Risk Symptoms administered as part of the SIPS interview.[43–45] Symptom ratings were less proximal to recordings in PRS, ranging from 170 days to the same day (mean = 23.6, SD = 25.5 days).

Procedure

Participants completed the Talk–Listen paradigm, described previously,[28] using Presentation software (www.neurobs.com/presentation). In the Talk condition, participants were trained to pronounce short (<300ms), sharp "ah" vocalizations repeatedly in a self-paced manner about every 1–2 s for 187s. Speech sounds were recorded and transmitted back to subjects through Etymotic ER3-A insert earphones in real time (0-ms delay). In the Listen condition, Talk condition recordings were played back and participants were instructed to listen. The number of "ah" sounds generated in the Talk condition was not significantly different across groups.

Data Acquisition and Preprocessing

EEG data were recorded from 64 channels using a BioSemi system (www.biosemi.com). EEG data were digitized at 1024 Hz and referenced offline to averaged earlobe electrodes before applying a 1-Hz high-pass filter using EEGlab.[35] Additional details of preprocessing, wavelet decomposition, and TF principal components analysis (PCA) appear in supplementary material.

To determine which TF components to analyze, we searched TF-PCA loadings and topographic maps of

associated factor scores for those in the theta band (figures 1A and 2A) with frontocentral "N1-like" topography, peaking in the first 200 ms after vocalization onset. This resulted in 1 ITC factor with a 125-ms, 5-Hz peak accounting for 17% of the variance (figure 1C) and 1 power factor with a 155 ms, 7-Hz peak accounting for 6% of the variance (figure 2C). Standardized, unitless factor scores for electrode Cz derived from these factors were subjected to further statistical analysis. TF-PCA provides an objective data-driven approach to quantifying TF activity in 2D space relative to averaging within some subjective temporal and spectral window.

Statistical Correction for Normal Aging

To control for normal brain maturation and aging effects, Talk–Listen difference scores at Cz for N1 amplitude, theta ITC, and theta power were regressed on age in HCs, and the resulting regression equations were used to calculate age-corrected z-scores for all groups. Note that because a "larger" N1 ERP component is more negative, difference scores were Talk minus Listen for N1, while theta ITC and power factor difference scores were calculated as Listen minus Talk. Thus, more suppression is associated with greater positive difference scores. The age-corrected z-scores were computed by subtracting the predicted score based on subjects' ages from their observed scores, and then dividing by the SE from the HC age-regression model. Resulting age-corrected z-scores reflect deviations from expected values for HCs at a specific age. Age-corrected z-scores are plotted in figures 1D and 2D for theta ITC suppression and power suppression, respectively. This method has been used previously[30,48] and is preferable to using age as a covariate in an ANCOVA model because it only removes normal aging effects, whereas ANCOVA could remove pathological aging effects from patient data.

Statistical Analysis

Main effects of suppression were assessed for all 3 measures in HCs using 1-sample *t*-tests on raw difference scores. Because the relationship between N1 suppression and age was previously shown to differ significantly between these groups,[30] we tested whether age relationships with theta ITC suppression and power suppression also differed between groups using general linear models (GLMs) with age, group, and group × age regressors. In these models, the group × age interaction tests for group differences in the slopes of age relationships. All remaining data analyses used age-corrected z-scores.

Age-corrected z-scores were assessed in a 3 × 3 repeated measures ANOVA using mixed models (SAS v9.4) with group (HC, ESZ, and PRS) as a between-subjects factor and measure (N1 suppression, theta ITC suppression, and theta power suppression) as a within-subjects factor.

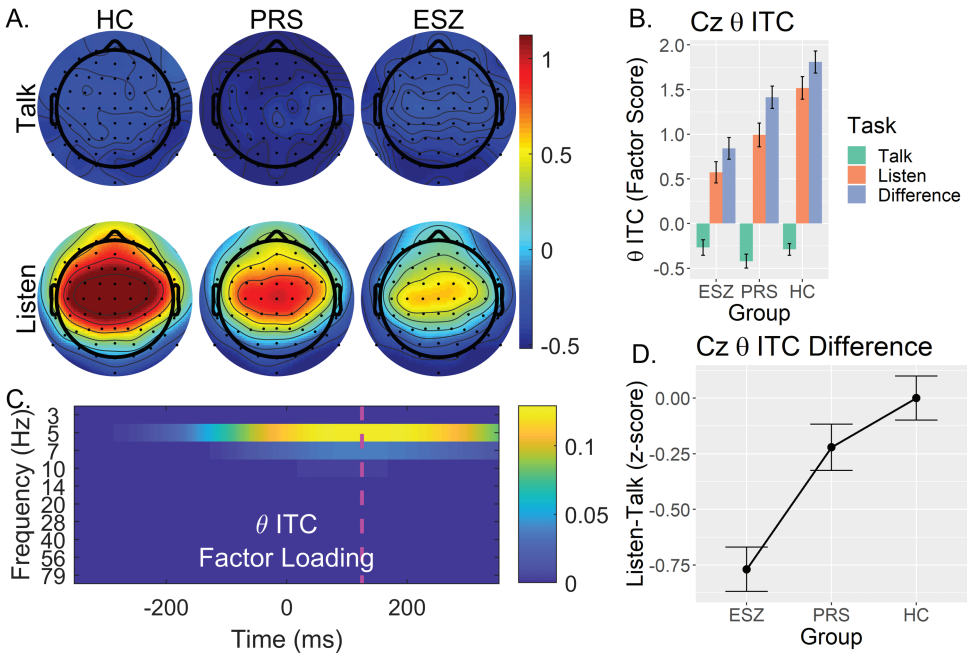

Fig. 1. Data representing the theta intertrial coherence (ITC) component from a Promax-rotated time-frequency factor analysis are shown. (A, top-left): Group average scalp topography maps for theta ITC factor scores are plotted for healthy control (HC), psychosis risk syndrome (PRS), and early illness schizophrenia (ESZ) groups for Talk (top) and Listen (bottom) conditions. (B, top-right): Mean ± SE bar graph depicting Cz factor scores show Talk, Listen, and Difference (Listen–Talk) effects for each group. (C, bottom-left): Time-frequency loading plot shows which frequencies contribute to this component, including 5 Hz and, to a lesser extent, 7 Hz, peaking at 125 ms after "Ah" stimulus onset. (D, bottom-right): Mean ± SE line graph of HC age-adjusted suppression z-scores. Negative values for ESZ and PRS groups represent theta ITC suppression reduction, in standardized units, relative to what is expected given subjects' ages.

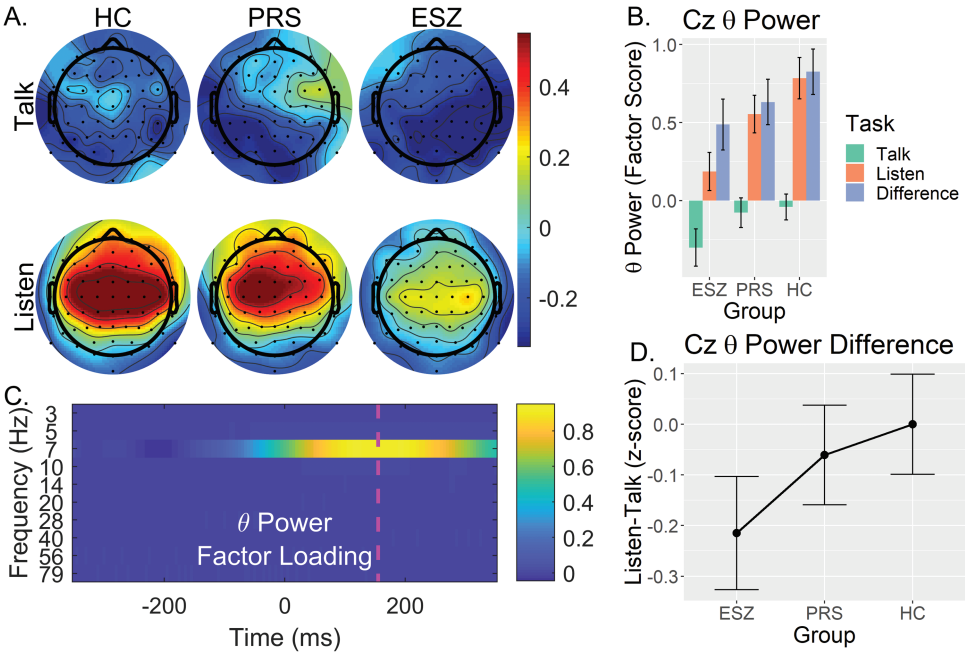

Fig. 2. Data representing the theta power component from a Promax-rotated time-frequency factor analysis are shown. (A, top-left): Group average scalp topography maps for theta power factor scores are plotted for healthy control (HC), psychosis risk syndrome (PRS), and early illness schizophrenia (ESZ) groups for Talk (top) and Listen (bottom) conditions. (B, top-right): Mean ± SE bar graph depicting Cz factor scores show Talk, Listen, and Difference (Listen–Talk) effects for each group. (C, bottom-left): Time-frequency loading plot shows that 7-Hz activity contributes to this component, peaking at 150 ms after "Ah" stimulus onset. (D, bottom-right): Mean ± SE line graph of the Cz electrode HC age-adjusted suppression z-scores. Negative values for ESZ and PRS groups represent theta power suppression reduction, in standardized units, relative to what is expected given subjects' ages.

Subject, nested within group, was treated as a random factor. An unstructured covariance matrix was used, allowing correlations between repeated measures to be estimated separately for each pair of measures within each subject group. Because of known group differences in N1 suppression[30] and interest in determining whether theta TF suppression measures outperform N1 suppression in discriminating between groups, planned contrasts were used to parse a significant group × measure interaction in this model. Specifically, to test if either theta ITC suppression or power suppression better differentiated between ESZ and HC than N1 suppression, 2 contrasts were run in which the ESZ–HC difference in N1 suppression was compared with each theta TF-suppression measure group effect. Two similar contrasts were conducted comparing HC–PRS group effects. Two contrasts (ESZ–HC and PRS–HC) were conducted to compare the group effect between theta power suppression and ITC suppression. In these contrasts, the null hypothesis is that the group difference in suppression for one measure is equal to the group difference in suppression for the other measure. This slightly differs from the typical null hypothesis (ie, that the group difference is 0) for follow-up group comparisons on each measure individually. Four additional contrasts (ESZ–HC and PRS–HC) were conducted to compare groups on theta TF-suppression measures as these have not been previously reported. These 10, nonorthogonal contrasts were Bonferroni corrected ($P = .005$).

To determine the extent to which N1 suppression could be accounted for by the theta TF-suppression measures, a GLM was implemented with group, ITC-suppression, and power-suppression z-scores as regressors. Before testing the common slope across groups, theta suppression × group interaction terms were included in a higher-order GLM to test for significant slope differences between groups for either theta suppression regressors. If these interaction terms did not significantly improve model fit, as evaluated with an R^2-change F-test, slope differences were assumed not to exist and the simplified GLM was used to predict N1 suppression. This GLM was also used to conduct ANCOVA-style tests of group differences in suppression z-scores, controlling for other suppression measures.

Given previously reported significant correlations between N1-suppression z-scores and unusual thought content in PRS, as well as lack of any significant correlations between N1-suppression z-scores and global positive symptom scores in ESZ,[30] tests for relationships between TF-suppression measures and positive symptom severity were conducted with 2 GLMs: (1) for PRS, unusual thought content and N1-suppression z-scores were regressors and, (2) for ESZ, all 4 global SAPS scores and N1-suppression z-scores were regressors. Each of these

models was applied to ITC-suppression and power-suppression z-scores and Bonferroni corrected ($P = .025$). In PRS, models were also run testing relationships between perceptual abnormalities and suppression. The N1-suppression z-scores served as a nuisance regressor in each model to remove any variance in symptom ratings associated with N1 suppression. This was done to avoid repeating derivative versions of suppression correlations from the previous paper, assuming non-zero correlations among suppression measures.

Results

Suppression Effects in HC

The well-established N1-suppression effect was clearly evident in HC as reported earlier[30] ($t(102) = 6.3825$, $P < .0001$). However, the N1-suppression effect size (Cohen's $d = 0.63$) was smaller than the ITC-suppression effect size (figure 1B; $t(102) = 14.7023$, $P < .0001$, Cohen's $d = 1.46$) but greater than power-suppression effect size (figure 2B; $t(102) = 5.6834$, $P < 0.0001$, Cohen's $d = 0.56$). The ITC-suppression effect size is double that for N1 suppresion and power suppression.

Group Differences in Suppression

Table 1 lists results of the ANOVA for group (HC, ESZ, and PRS) and measure (N1 suppression, power suppression, and ITC suppression). There were significant effects of group, measure, and a group × measure interaction. The interaction was parsed with planned contrasts described above and listed in table 1. These contrasts revealed that the HC–PRS difference was greatest for N1 suppression, but this difference was not greater than either theta ITC suppression ($P = .5492$) or power suppression ($P = .1296$). The HC–ESZ difference was greatest for theta ITC suppression, but this difference was not significantly greater than the N1-suppression effect ($P = .0956$). Like HC–PRS, the N1 suppression for the HC–ESZ difference was nonsignificantly greater than the theta power-suppression difference ($P = .11$). The group differences between theta-suppression measures were equivalent for HC vs PRS ($P = .351$), but the HC–ESZ comparisons revealed that theta ITC suppression significantly outperformed power suppression ($P = .0015$). The HC–ESZ difference in ITC suppression was significant ($t(510) = 5.6$, $P < .0001$), but the HC–PRS difference in ITC suppression was not ($t(510) = 1.54$, $P = .1239$). Power suppression did not differ between groups (all Ps $> .198$). This pattern of group differences is plotted in supplementary material using Cohen's d statistics (supplementary figure S1). Results were unchanged when raw scores and age-matched groups were used in alternative contrasts.

Table 1. Group Differences in Suppression

Type 3 tests of fixed effects				
Effect	Num *df*	Den *df*	*F*-statistic	*P*-value
Group	2	255	11.76	<.0001
Measure	2	510	5.7	.0036
Group × measure	4	510	3.38	.0095

Follow-up tests of pairwise group differences					
Contrast	Estimate	SE	*df*	*t*-statistic	*P*-value
HC vs PRS, N1 vs ITC	−0.09739	0.1625	510	−0.6	.5492
HC vs ESZ, N1 vs ITC	0.2648	0.1586	510	1.67	.0956
HC vs PRS, power vs N1	0.2582	0.1701	510	1.52	.1296
HC vs ESZ, power vs N1	0.3009	0.188	510	1.6	.11
HC vs PRS, power vs ITC	0.1608	0.1723	510	0.93	.351
HC vs ESZ, power vs ITC	0.5657	0.1767	510	3.2	.0015

Note: df, degrees of freedom; HC, healthy control, PRS, psychosis risk syndrome, ESZ, early illness schizophrenia; ITC, intertrial coherence.

Predicting N1 Suppression From Theta Suppression

The N1-suppression z-score was the dependent variable in a GLM including group and TF-suppression measures as predictors. The group × ITC suppression and group × power suppression interaction terms were entered in a higher-order GLM. The R^2-change test was not significant ($F(4,253) = 1.1917$, $P = .315$, R^2 change = 0.0149), indicating that the slopes of the relationships between N1-suppression and TF-suppression measures were not different between groups. The common slopes for both theta ITC suppression and power suppression, controlling for each other and group, were tested in the reduced GLM. Each TF-suppression measure showed significant, independent positive associations with N1 suppression, but the magnitude of the relationship with theta ITC suppression ($\hat{\beta} = .365$, $t(253) = 5.926$, $P < .0001$) was more than double the power-suppression relationship ($\hat{\beta} = .139$, $t(253) = 2.31$, $P = .022$; Scatterplots are shown in supplementary figure S2). This model accounted for 21% of N1-suppression variance.

This GLM was used to test for a main effect of Group on N1 suppression, controlling for theta ITC suppression and power suppression. There was no significant main effect of group (table 2). Using a similar GLM approach to determine if theta ITC suppression was still sensitive to group, controlling for other suppression measures, revealed a significant effect of group, driven by HC having more ITC suppression than ESZ ($t(253) = 4.45$, $P <$

.0001) but not PRS ($t(253) = 0.78$, $P = .43$). The power-suppression GLM was nonsignificant (table 2).

Positive Symptom Severity Correlations With Theta Suppression

ITC suppression was regressed on positive symptoms in ESZ while controlling for N1 suppression. Only delusion severity was correlated with ITC suppression ($\hat{\beta} = -.176$, $t(75) = -2.736$, $P = .007$), controlling for the other positive symptoms (hallucinations, formal thought disorder, and bizarre behavior), and N1 suppression. That is, patients with more severe delusions have less theta ITC suppression (figure 3). This analysis was repeated for Talk and Listen theta ITC separately, revealing that neither theta ITC during Talk ($P = .06$) nor Listen ($P = .20$) were related to delusion severity. While it appears that the sensitivity of ITC suppression to schizophrenia is driven by ITC during playback (see figure 1), Listen does not drive the relationship with delusion severity in ESZ. Power suppression was not related to symptoms.

Unlike the relationship between N1 suppression and unusual thought content ($r = -.404$, $P = .0006$) in the PRS sample,[30] neither ITC suppression ($t(66) = 1.698$, $P = 0.09$) nor power suppression ($t(66) = 0.993$, $P = .3243$) were related to unusual thought content, controlling for N1 suppression. Likewise, neither ITC suppression ($t(66) = -1.229$, $P = .223$) nor power suppression ($t(66) = 1.327$, $P = .189$) were related to perceptual abnormalities.

Table 2. Analysis of Covariance (ANCOVA)

ANCOVA group effects				
Dependent variable	Num *df*	Den *df*	Statistic	*P*-value
N1 suppression	2	253	$F = 1.712$	.183
ITC suppression	2	253	$F = 10.747$	<.0001
HC vs. PRS	1	253	$t = 0.783$	.434
HC vs. ESZ	1	253	$t = 4.445$	<.0001
Power suppression	2	253	$F = 0.023$	.977

Note: Abbreviations are explained in the first footnote to table 1.

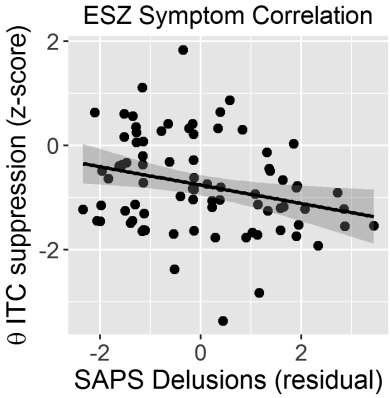

Fig. 3. Scatter plots showing the relationship between theta intertrial coherence (ITC) suppression z-scores and delusion severity. Note: Scale for the Assessment of Positive Symptoms (SAPS) global delusion symptom rating scores (*x*-axis) represent residualized scores controlling for the effects of N1 suppression (z-score) and other SAPS global rating scores (ie, hallucinations, formal thought disorder, and bizarre behavior).

Effects of Age on Suppression

We previously reported a significant, positive relationship between N1 suppression and age in HC but a significantly reduced relationship in ESZ.[30] Similar models for theta ITC suppression and power suppression revealed no group × age interactions and modest positive associations with age and suppression across all groups (theta ITC suppression: $t(253) = 1.97$, $P = .0496$; theta power suppression: $t(253) = 2.14$, $P = .0337$). See details in supplementary material.

Discussion

Because N1 comprises both theta ITC and theta power, we asked if they might also be suppressed during talking compared to listening like N1 is. Indeed, they are. In fact, theta ITC suppression's effect size is more than twice that of N1 suppression and theta power suppression in HCs. We next asked if theta ITC suppression and power suppression are sensitive to schizophrenia and psychosis risk, like N1 suppression in this sample.[30] ITC suppression distinguishes the HC and ESZ and has a larger effect size (Cohen's $d = 0.8$) than N1 suppression (Cohen's $d = 0.49$). When controlling for the other measures, only theta ITC suppression distinguishes between groups. This effect is due to deficient theta ITC suppression in ESZ, not in PRS. Importantly, when deprived of the variance shared with theta ITC suppression and power suppression, N1 suppression was no longer sensitive to differences between either HC and ESZ or HC and PRS. That theta ITC measures make unique contributions to our understanding of psychosis pathophysiology in this study is consistent with others[49–53] who suggested that theta phase may provide more information about auditory processing and better reflect differences between schizophrenia patients and controls than averaged ERPs.

We suggest that deficits in theta ITC suppression may be a biomarker of schizophrenia, while deficits in N1 suppression may be a biomarker of more general psychosis vulnerability; it is apparent in patients with schizophrenia,[10,12,54] psychotic bipolar patients,[12] patients with schizoaffective disorder,[12] nonhelp-seeking people with schizotypy,[29] and PRS samples[30] and it is reduced at intermediate levels in unaffected first-degree relatives of patients with schizophrenia, psychotic bipolar disorder, and schizoaffective disorder.[12]

We suggest that the phase of ongoing theta oscillations in the auditory cortex is reset when externally generated

sounds are heard, alerting us that they may be important. This phase resetting contributes to the emergence of the N1 seen at the scalp. We further suggest that, during talking, a corollary discharge of the motor command is sent to the auditory cortex.[13,14] This signal may inhibit phase resetting, minimizing the alerting quality of the sound, and reducing N1 amplitude.

While N1 suppression is correlated with both theta ITC suppression and power suppression, much variance is unaccounted for. That is, there is more to N1 suppression than theta ITC suppression and power suppression. In addition to the event-related perturbation of the ongoing theta oscillations in the EEG, N1 amplitude may contain an evoked auditory signal, potentially obscured by so-called induced or other (spontaneous) nonphase-locked power in the ongoing EEG. It is also likely that perturbation of other frequencies contributes to N1 amplitude and its suppression during talking. That is, N1 is a complex component, which can be decomposed into simpler elements. We have shown that TF decomposition of N1 provides a more precise assessment of neural responses associated with the corollary discharge mechanism in our talking paradigm. Perhaps because of its precision, theta ITC suppression has a clearer relationship to delusion severity.

We might ask why theta power suppression does not also emerge as a superior biomarker to N1 suppression in this study. Like N1, our measure of power is also complex and includes both evoked power and so-called induced changes in power, relative to baseline. Possibly, the induced theta band oscillations are less affected by our conditions, making it a lesser assay of corollary discharge. Importantly, ITC is calculated using amplitude-normalized phase angle values such that theta power does not influence it, and it provides a simpler, more distilled measure of cortical excitability.

Variation in the phase of neural oscillations from trial to trial rather than variation in amplitude may be critical to a veridical experience of our environment and the sensations our actions generate. Bland and Oddie[39] suggested that systems underlying the production of hippocampal theta are key in providing voluntary motor systems with continually updated feedback on their performance. While scalp EEG recordings are insensitive to hippocampal activity, electrophysiological studies of animals moving and generating the sensations they experience may help fill this gap in our understanding of the prominence of theta synchrony over power in our studies of corollary discharge.

In conclusion, people with schizophrenia often misperceive sensations and misinterpret experiences, perhaps contributing to delusions. This may result from a basic inability to make valid predictions about expected sensations resulting from their own actions. Healthy normal people take advantage of neural mechanisms that allow them to make predictions unconsciously and quickly, facilitating the processing of sensations and distinguishing the expected from the unexpected. If predictive mechanisms, such as the corollary discharge, are dysfunctional, sensations that should have been predicted, but were not, might take on inappropriate salience.[55] Our talking paradigm may serve as an assay of this elemental mechanism with far-reaching consequences for veridical experiences of the world, and our distilled reflection of auditory cortical activity may provide important information about this predictive mechanism.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin* online.

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