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Cognitive, clinical, and environmental moderators of auditory processing impairment and its improvement in first-episode schizophrenia

A dissertation submitted in partial satisfaction of the

requirements for the degree Doctor of Philosophy

in Psychology

by

Emily Louise Martinez Nesi

2026

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ABSTRACT OF THE DISSERTATION

Cognitive, clinical, and environmental moderators of auditory processing impairment and its improvement in first-episode schizophrenia

by

Emily Louise Martinez Nesi

Doctor of Philosophy in Psychology

University of California, Los Angeles, 2026

Professor Cindy M. Yee-Bradbury, Chair

Cognitive symptoms of schizophrenia can be substantially improved with cognitive training (CT) interventions, such that durable cognitive gains emerge along with strengthening of relevant neural circuits. However, treatment response is often variable, and optimizing CT efficacy likely requires a deeper understanding of the pathophysiological processes associated with cognitive impairment in schizophrenia. Early auditory processing impairments, involving stimulus registration and sensory gating, are well established in schizophrenia. Further, these auditory impairments have demonstrated relationships with cognitive symptoms and may be indirectly strengthened through CT, though a range of internal and external factors may also influence these effects. Across three studies, the present dissertation examined auditory processing impairments and their potential predictors and consequences in adults experiencing a first

episode of schizophrenia. Participants with schizophrenia and healthy comparison participants completed EEG recordings during a paired-stimulus procedure, along with clinical and neurocognitive assessments. Patients were evaluated before and after participation in a CT intervention. Event-related brain potentials (ERPs) derived from EEG data were used to characterize auditory processing in both cross-sectional and longitudinal analyses. Findings from Study 1 supported a combined model of sensory gating impairment in schizophrenia, reflecting both poorer registration of initial stimuli and less suppression of repeated stimuli. However, no systematic changes in auditory ERPs were observed following CT. Studies 2 and 3 examined potential sources of group- and individual-level variability in auditory and cognitive trajectories by testing the moderating effects of internal (auditory hallucinations) and external (noise pollution) factors. Study 2 demonstrated that sensory gating impairments were more pronounced in patients experiencing recent and persistent auditory hallucinations. Study 3 found evidence of larger between-group differences in sensory gating among participants exposed to high levels of environmental noise. Neither of the two factors accounted for significant variance in auditory or cognitive change trajectories, however. Although findings across the three studies were somewhat mixed, they collectively provide preliminary support for an integrated model of auditory dysfunction in schizophrenia and offer direction for future research aimed at identifying moderators of intervention response trajectories.

The dissertation of Emily Louise Martinez Nesi is approved.

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2026

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Sargent, K.S., **Martinez, E.L.**, Reed, A.C., Guha, A., Bartholomew, M.E., Diehl, C.K., Chang, C. S., Salama, S., Popov, T., Thayer, J. F., Miller, G.A., & Yee, C.M. (2024). Oscillatory coupling between neural and cardiac rhythms. Psychological Science, 35(5), 517-528.

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General Introduction

Schizophrenia is a severe mental illness that typically involves intermittent periods of acute psychosis interspersed with chronic disturbances in emotional, behavioral, and cognitive functioning. Symptoms of schizophrenia can be classified into three major clusters: positive symptoms (e.g., hallucinations and delusions), which are often the primary targets of pharmacological and psychotherapeutic interventions; negative symptoms (e.g., anhedonia, avolition, alogia), which can also be highly debilitating and interfere with daily functioning (Marder & Galderisi, 2017); and cognitive symptoms (e.g., impairments in attention, working memory, processing speed), which are often the least responsive to intervention (Lally & MacCabe, 2015) and the strongest predictors of long-term functioning and quality of life (Green et al., 2004).

A number of treatments are available for ameliorating positive symptoms (Shergill et al., 1998; Zimmermann et al., 2005) and to a lesser degree, negative symptoms (Correll & Schooler, 2020), whereas few exist for improving cognitive symptoms. Cognitive remediation therapies, or cognitive training (CT), address cognitive symptoms by gradually retraining core building blocks of cognition, utilizing principles of learning and neuroplasticity to strengthen associated brain circuits and promote stable cognitive gains (Best & Bowie, 2017; Bowie et al., 2020). Optimizing the efficacy of CT likely depends on a thorough understanding of the pathophysiological processes that are associated with cognitive impairment and improvement in patients with schizophrenia (Fisher et al., 2016; Vinogradov et al., 2012).

As with any intervention, patients do not demonstrate uniform improvement with CT. It is therefore imperative to examine patient trajectories and evaluate whether and which pre-illness or pre-intervention factors predict a greater or lesser response to standardized CT interventions.

Such an approach can serve to inform future prospective treatment studies that integrate pre-illness measurements into an intake evaluation and to personalize treatments based on biomarkers, experiences, and environments.

A core set of impairments in schizophrenia that may contribute to the clinical and cognitive symptoms of the illness include those involving sensation, perception, and information processing (Javitt & Freedman, 2015). These processes are the avenues by which information from the environment is taken in and utilized to support individual functioning and goals. Numerous studies examining sensory-perceptual systems while relying on a variety of methods have consistently demonstrated breakdowns in how information is encoded and used in schizophrenia (see Javitt, 2009a, for a brief review). In particular, the auditory system has been implicated in models of dysfunctional processes, perhaps due to the higher prevalence of auditory hallucinations relative to other sensory domains among individuals experiencing positive symptoms of psychosis (McCarthy-Jones et al., 2017), or the close synergy between auditory and language networks in the brain (Gierhan, 2013) and the role of thought and language in primary symptoms of schizophrenia (X. Chang et al., 2022), or a combination of these factors. In schizophrenia, auditory processing impairments can range from relatively basic auditory sensory functions (e.g., inaccurate registration of incoming auditory information; Dondé et al., 2023) to more coordinated auditory perceptual functions. Well-established deficits in coordinated functioning include a reduced ability to filter out or inhibit processing of extraneous auditory information to facilitate responding to more pertinent inputs, a process known as auditory sensory gating (Adler et al., 1982). Dysfunction in either or both sets of functions can result in the passing of noisy information to higher-level cognitive processing areas, compounding the effects of the disruption (Javitt, 2009a).

Auditory processing impairments in schizophrenia are commonly examined using neurophysiological methods (e.g., EEG, MEG, acoustic startle response, and MRI), which inform theories about brain structures and mechanisms that are implicated in both lower-level and higher-order auditory dysfunction. These approaches, in turn, permit exploration of potential predictors and consequences of auditory processing impairments and allow researchers to contextualize sensory and perceptual impairments within the greater clinical conceptualization of the illness and its associated pathophysiology. For example, EEG has excellent temporal resolution and can precisely capture changes in the brain's electrical activity evoked by an auditory stimulus or event. Various event-related brain potentials (ERPs) that index early auditory processing have been identified and are consistently shown to be atypical in schizophrenia (Bramon et al., 2004; Rissling & Light, 2010; Rosburg et al., 2008; Shen et al., 2020) and associated with cognitive symptoms of the illness (Hamilton et al., 2018; Koshiyama et al., 2021).

Interventions that rely on CT to target early auditory processing have been shown to result in improvements in auditory functioning as well as cognition (C. L. Dale et al., 2015; Fisher et al., 2016; Medalia et al., 2019; Popov et al., 2011). However, it remains unclear whether these improvements are specific to the facets of auditory processing that are being targeted or whether broader, non-specific auditory plasticity can be induced. Further, schizophrenia is a highly heterogeneous disorder and not all individuals with the illness will exhibit uniform impairments in early auditory processing or cognition. For certain individuals, CT may be more effective in inducing cognitive and/or auditory improvement by taking various factors into consideration, including but not limited to baseline sensory and perceptual

processing, broader auditory-related clinical and cognitive symptom profiles, and environmental influences during the training period.

The present dissertation was designed to clarify the pathophysiology associated with schizophrenia by characterizing auditory processing impairments and their potential predictors and consequences in a sample of adults experiencing a first episode of illness and who underwent a CT intervention. Study 1 investigated the extent to which ERP components that index early auditory attentional and perceptual processing (specifically, P50 and N100) improve with CT and whether baseline auditory functioning predicts an individual's treatment-related cognitive gains. Study 2 examined whether auditory processing impairments in schizophrenia are related to other clinical symptoms involving aberrant auditory salience processing, specifically auditory hallucinations, and if auditory ERP components covary with changes in symptom state. Study 3 explored whether auditory ERP improvement associated with CT is moderated by concurrent exposure to environmental noise pollution, which was proposed to interfere with plasticity-related gains and result in disproportionately poorer outcomes for individuals who live in regions with high levels of transportation-related noise, thus representing an important public health target. Taken together, these three studies aimed to identify correlates and boundaries of auditory and cognitive improvement in first-episode schizophrenia.

Study 1: Relationships between Intervention-Related Changes in Early Auditory Processing and Cognitive Functioning

Cognitive and Auditory Impairment in Schizophrenia

Although not specified explicitly in the Diagnostic and Statistical Manual for Mental Disorders, 5th Edition (DSM-5) criteria for schizophrenia, cognitive impairments are exhibited by nearly all individuals with the illness and result in levels of functioning that are moderately to severely impaired relative to pre-illness estimates (Keefe & Harvey, 2012). Cognitive impairments can span the domains of attention, memory, learning, processing speed and efficiency, reasoning, problem-solving, and social cognition (Nuechterlein et al., 2004), each of which may contribute to difficulties in social and occupational functioning (Bowie & Harvey, 2005; Brekke et al., 2005) but in ways that vary across individuals (Habtewold et al., 2020). Factor analyses and other statistical approaches have demonstrated that, despite significant overlap between cognitive domains, they represent distinct areas of functioning and impairment (Gold et al., 2018; Knowles et al., 2015; Nuechterlein et al., 2004) and ostensibly relate to distinct patterns of pathophysiological disturbances.

Efforts to uncover the causes of these disturbances typically focus on modeling associations between diverse aspects of cognition and associated neural systems (Barch, 2005). Many models of cognitive functioning are based on a "bottom-up," hierarchical framework involving sensation, perception, and cognition, wherein information at a higher level has been fed through (and preprocessed at) lower levels (Marchi, 2020). For the auditory system, incoming information from the environment travels through auditory nerve fibers and subcortical processing structures to primary auditory cortex, where it is processed before being sent to association areas and prefrontal cortex for use in supporting cognitive functions (Mesulam, 1998). According to these models, breakdowns in the integrity of auditory processing in primary

auditory cortex could feed forward to other regions (e.g., prefrontal cortex) and result in disruptions to cognitive processing (Javitt, 2009b). At the same time, auditory processing can be modulated via "top-down" cognitive processes, including attention and working memory systems, which can exert an influence on which information in primary auditory cortex is attended to and processed further (Fritz et al., 2007). The potential for bidirectionality underscores the challenge in disentangling causal influences within and between patterns of impairment in disorders involving cognitive dysfunction.

Schizophrenia is associated with wide-ranging patterns of auditory processing impairments, observed both early and late in the processing stream and affecting both automatic and controlled forms of activity. Stimulus registration is consistently shown to be impaired in experimental studies of schizophrenia (Rissling & Light, 2010). In a recent review, Fivel et al. (2023) reported that 80% of studies examining group-level differences in basic discrimination of tonal pitch, sound intensity, stimulus duration, and sound localization showed significantly poorer performance in individuals with schizophrenia than in healthy comparison participants. Early auditory impairments are also seen in more coordinated processes, including "sensory gating" or the capacity to inhibit processing of certain inputs in order to facilitate the processing of others that are more novel, relevant, or salient (Javitt & Freedman, 2015). The impact of early auditory impairments can be carried later into the processing stream, interacting with higher-order systems and emerging as disruptions to speech and language processing (Niznikiewicz et al., 1997) and self-monitoring and predictive coding (Bansal et al., 2018a).

Much of the research on early auditory processing impairments in schizophrenia uses electroencephalography (EEG) to examine millisecond-level changes in the brain's electrical activity in response to an auditory stimulus or event. EEG can be analyzed in the form of event-

related brain potentials (ERPs), with specific scorable components that have been empirically validated as manifestations of physiological phenomena supporting perceptual and cognitive processes. Two ERP components of specific relevance to early auditory processing and cognitive symptoms of schizophrenia are P50 and N100.

P50 Event-Related Potential Component

The auditory P50 ERP component is a scalp-positive voltage deflection that occurs approximately 50 ms after the onset of an auditory stimulus. P50 is typically examined using a paired-stimulus passive listening paradigm, during which brief identical stimuli are presented in quick succession (500 ms apart) within each pair. The proposed P50 mechanism is that registration of the first stimulus (S1) triggers an automatic inhibitory cascade that suppresses a response to the redundant information conveyed by the second identical stimulus (S2). Accordingly, P50 amplitude to S2 is typically smaller than P50 amplitude to S1, reflecting successful inhibition of processing of repeated sensory input. P50 responses to S1 and S2 can be combined into a single ratio metric (P50 amplitude to S2/P50 amplitude to S1), with a smaller ratio score reflecting stronger auditory inhibition or P50 gating.

In schizophrenia, P50 amplitude to S2 typically shows less or no reduction and results in higher P50 ratio scores than in healthy individuals, which is interpreted as evidence that the inhibitory gating mechanism is not fully activated in response to redundant stimuli. Impairment in P50 suppression or P50 inhibitory gating is a robust finding in the research literature on schizophrenia (Bramon et al., 2004; Heinrichs, 2004; Patterson et al., 2008). However, there are mixed results regarding whether elevated P50 ratio scores in schizophrenia are primarily driven by a smaller-than-typical S1 response, a larger-than-typical S2 response, or a combination of the

two (Brenner et al., 2009; W.-P. Chang et al., 2011; Patterson et al., 2008; A. K. Smith et al., 2010).

P50 gating has been conceptualized as a measure of preattentional processing of auditory information, reflecting a hard-wired and entirely stimulus-driven response that is not influenced by voluntary attention in healthy individuals (Freedman et al., 1987; Jerger et al., 1992; White & Yee, 1997). The P50 gating impairment in schizophrenia was similarly thought to be a hard-wired, automatic failure of inhibition (Adler et al., 1982; Freedman et al., 1987; Nagamoto et al., 1991), suggesting a fixed and unmalleable deficit. In contrast to this theory, Yee et al. (2010) demonstrated that P50 gating in schizophrenia can be enhanced by directing voluntary attention to S1. By supplementing the preattentional S1 processing with voluntary attention toward S1, individuals with schizophrenia showed transient improvements in P50 gating ratio scores largely driven by reductions in S2 responses and not by enhancements in S1 responses. These findings were taken as evidence that enhanced directed attention to S1 initiated the inhibitory cascade in a manner similar to what is seen in healthy participants. Conversely, directing attention to S2 in healthy individuals was shown to disrupt P50 gating, resulting in worsening of P50 ratio scores (Guterman et al., 1992; Yee et al., 2010). By intentionally failing to inhibit a response to the repeated stimulus, healthy individuals demonstrated transient impairments in P50 gating in a manner similar to what is seen in schizophrenia, further supporting this coordinated inhibitory model of gating.

A number of studies have supported a relationship between P50 gating and attention in schizophrenia and extended the association to different aspects of cognition. For example, poorer P50 suppression is associated with higher scores on clinician-rated inattentiveness as well as poorer performance on neurocognitive assessments of attention, working memory, and

processing speed (Hamilton et al., 2018; A. K. Smith et al., 2010; Thoma et al., 2006; Yee et al., 1998). These interrelated findings suggest that P50 gating impairments (and early auditory inhibitory processing impairments more broadly) may be amenable to improvements with interventions that target early attention and other cognitive functions.

N100 Event-Related Potential Component

The auditory N100 component is a scalp-negative voltage deflection occurring approximately 100 ms post-stimulus onset that can be evoked during both passive and active task paradigms. In passive listening designs, N100 is typically used to index voluntary allocation of attentional resources toward an auditory input (Hillyard et al., 1973; Picton et al., 1971), though it is also sensitive to acoustic features of the stimulus presentation (Rosburg et al., 2008). N100 amplitudes are consistently reduced in schizophrenia and interpreted as evidence of impaired orienting to novel auditory information (Rosburg et al., 2008; Shen et al., 2020). In one study, reduced N100 amplitudes reliably differentiated patients diagnosed with schizophrenia from those diagnosed with bipolar disorder and healthy comparison participants (Force et al., 2008), suggesting a mechanism of impaired auditory stimulus registration that is unique to, or perhaps more pronounced in, schizophrenia.

There is some evidence of an N100 suppression or N100 gating impairment in schizophrenia in the context of the paired-stimulus passive listening paradigm (Boutros et al., 2009), but meta-analyses suggest that this apparent gating impairment is largely reflective of a smaller N100 to S1 rather than a failure to gate S2 (Rosburg, 2018). Though N100 amplitudes are primarily associated with attention, they also correlate with other domains of cognitive functioning in schizophrenia. In one study, N100 amplitude to the first stimulus in a pair was associated with better performance on measures of attention, working memory, and long-delay

memory, but only the association with attention remained significant after controlling for general intellectual functioning (A. K. Smith et al., 2010).

Capacity for Improvement: Remediation and Plasticity

In light of the relationships between P50 gating, N100 amplitude, and cognitive symptoms of schizophrenia, early auditory processing impairments may be mechanistically linked to cognitive symptoms and represent one of the core building blocks that are strengthened by cognitive training (CT). Indeed, models of cognitive remediation generally hold that disruptions manifesting at the highest levels of cognition can be a representation of impairment at any of the subordinate levels. Thus, including subordinate levels in efforts to remediate cognitive impairments may be highly valuable (Vinogradov et al., 2012). At the same time, remediation at higher levels may generalize into observable improvements at lower levels (Best & Bowie, 2017), such as attentional or auditory systems, because of feedback relationships between levels.

Many CT protocols are designed to engage physiological learning systems via patterning and repetition, thereby harnessing the brain's innate plasticity to promote the strengthening of neural systems that support various cognitive domains (Adcock et al., 2009; Fisher et al., 2009, 2016; Popov et al., 2011, 2012, 2015; Vinogradov et al., 2012). This approach is consistent with the bottom-up view of cognition, with core building blocks of cognition being gradually retrained to support coordinated, higher-order functioning. In practice, computerized CT modules are typically designed with a given higher-order cognitive system in mind (Fisher et al., 2009, 2016; Popov et al., 2011, 2012, 2015; Vinogradov et al., 2012). Implicit in the design of these higher-order modules is the assumption that the associated neural systems will be reliably engaged, potentially including those that support early auditory processing. If this model holds

true, training-related changes in cognitive symptoms could be associated with corresponding improvements in early auditory processing, resulting in functional changes to the impaired auditory system via auditory neuroplasticity (Irvine, 2018).

There have been efforts to improve the design of CT protocols so as to better target mechanisms of cognitive dysfunction at multiple levels, but the mixed findings reported in many studies suggest a potential tradeoff between specificity of training and magnitude of cognitive gains (Best & Bowie, 2017). Many studies have specifically focused on relationships between CT and auditory plasticity. For example, Popov et al. (2011, 2015) demonstrated that "function-specific training" that targeted auditory perceptual skills resulted in improvements to ERP measures of auditory information processing (P50 gating ratio and N100) and their magnetic analogs (M50 gating ratio and M100) and in improvements in cognition, although cognitive changes were not specific to the function-specific training. More specifically, the targeted intervention successfully fostered auditory plasticity, but the auditory changes did not translate to enhanced cognitive functioning above and beyond a standard CT intervention. Medalia et al. (2019) found that CT emphasizing early auditory processing induced changes in auditory functioning but benefitted only the verbal learning cognitive domain, and only among patients who demonstrated baseline auditory impairments. Therefore, it is unclear whether the added investment in focusing on the specific target of auditory processing is advisable for ameliorating broad cognitive symptoms and their associated patterns of dysfunction, or whether such a tailored approach would be best reserved for certain individuals.

At the same time, evidence linking cognitive performance in schizophrenia to early auditory information processing (e.g., Koshiyama et al., 2021) supports continued examination of ways to measure auditory perceptual changes that are associated with CT. It is possible that

broad forms of CT that include, but do not narrowly target, auditory skill development (e.g., Nuechterlein et al., 2014) are capable of guiding auditory plasticity by fostering the capacity to attend to, extract information from, and selectively inhibit auditory signals in a strategic manner. Plasticity in auditory cortical neurons could be harnessed by repetitive learning paradigms and modulated by higher-order cortical regions (e.g., attention networks) in order to optimize auditory performance (Irvine, 2018).

The bidirectional relationships between early auditory and more general cognitive processing described thus far suggest that improvements in general attentional and executive functioning via broad or non-targeted CT may lead to downstream improvements in the early processing of stimulus information (as measured with P50 and N100) and sensory gating (as measured with the P50 ratio score). However, it is unclear whether this mechanism of top-down strengthening of bottom-up auditory processing would occur to the same extent for all patients, particularly those with poorer auditory functioning at baseline. For these individuals, the indirect effects of broad CT on auditory plasticity may not be as potent, such that an auditory-targeted form of CT (e.g., Medalia et al., 2019; Popov et al., 2011, 2015) would be better suited to foster auditory plasticity and enhance cognitive gains.

Study Overview & Hypotheses

Study 1 sought to characterize the relationship between auditory processing impairments and cognitive impairments in first-episode schizophrenia, particularly with respect to whether longitudinal, treatment-related improvements covary between the two. More specifically, the goal of Study 1 was to evaluate whether a systematic CT intervention that included but did not specifically target auditory perceptual skills would be capable of inducing changes in ERP markers of early auditory processing, and to determine whether such auditory improvements

differentially predicted improvements in certain subdomains of cognition. EEG and cognitive symptom data were collected from patients recently diagnosed with schizophrenia and demographically-matched healthy comparison participants before and after patients completed a six-month CT intervention that incorporated both bottom-up (e.g., basic auditory and attentional functioning) and top-down (e.g., executive functioning) skills (Nuechterlein et al., 2014). By relying on an early-illness sample, this study sought to determine mechanisms of learning-induced changes in brain and behavior that may be unique to treatments offered during the early phase of schizophrenia.

Data were analyzed at baseline prior to introducing CT to replicate prior work examining auditory and cognitive impairments in schizophrenia, then longitudinally to examine intervention-related changes in auditory and cognitive outcomes, as well as their associations. Consistent with the literature reviewed above, it was expected that the schizophrenia group would have smaller average P50 and N100 amplitudes to S1 and a larger average P50 gating ratio score at baseline than the healthy comparison group, and that individual auditory ERP measures would correlate with performance-based and clinician-rated measures of cognitive functioning. The CT intervention was also expected to foster sufficient auditory plasticity for the schizophrenia group, as measured by reductions in P50 ratio scores and enhancements in P50 and N100 amplitudes to S1 at follow-up relative to baseline.

Consistent with the view that individuals with more pronounced impairments in early auditory processing may require a more targeted intervention to promote auditory plasticity, it was hypothesized that individuals with larger baseline P50 ratio scores and smaller baseline P50 and N100 amplitudes to S1 would exhibit a weaker auditory response to the broad CT intervention; specifically, a smaller magnitude of ERP improvement would be observed than in

individuals with more intact baseline auditory processing (smaller P50 ratio scores and larger P50 and N100 amplitudes to S1). Finally, with respect to the proposed relationship between cognitive and auditory improvement, it was predicted that patients whose cognitive symptoms demonstrated a stronger response to the CT intervention would correspondingly show more improvement in auditory ERPs, with auditory changes predicting cognitive changes. It was further predicted that the strength of these cognitive-auditory relationships would differ across cognitive domains. Given the reviewed literature consistently associating attention, P50, and N100, the strongest relationships were expected between auditory ERP and attentional gains.

Method

Participants

Participants were recruited as part of a clinical trial (NIMH R01 MH110544) that was integrated with a project focused on specifying neurobiological mechanisms associated with clinical and cognitive improvements following CT (R01 MH110544-S1). Seventy-four participants with schizophrenia (abbreviated SZ in following sections) and 41 demographically-matched healthy comparison (abbreviated HC in following sections) participants were included in the present study. Six-month follow-up data were available for 30 (41%) and 27 (66%) participants from each group, respectively, with a higher proportion for the comparison group, Yates-corrected $\chi^2(1) = 5.79$, $p = .016$. Whereas both groups experienced attrition due to COVID-19-related interruptions in follow-up visits and unspecified voluntary discontinuation of the EEG study, the SZ group had additional and unique sources of attrition, including patients completing baseline testing but not ultimately enrolling in the larger clinical trial, or enrolling in the trial but discontinuing CT early. In both of these scenarios, SZ participants could not be included in follow-up testing. However, there was no significant interaction between group and follow-up

status (baseline-only or returned for follow-up) for any baseline auditory or cognitive outcome measures, suggesting minimal differences within the domains of interest for this study between those who did and did not return for follow-up.

Participants with SZ were recruited from the UCLA Aftercare Research Program, an outpatient research clinic for individuals who recently experienced a first episode of psychosis. Patients included in the study met *DSM-5* criteria for schizophrenia, schizophreniform disorder, or schizoaffective disorder, depressed type, confirmed using the Structured Clinical Interview for *DSM-5*, Research Version (SCID-5-RV; First et al., 2015) during intake evaluations conducted by clinic staff. All patients were receiving antipsychotic medication and case management and were clinically stabilized over a period of approximately three months prior to study enrollment. All 30 SZ participants with six-month follow-up data available completed the same CT intervention. As part of the R01 clinical trial, 15 of these patients received aerobic exercise training and the other 15 received instruction on healthy living skills (e.g., wellness, nutrition, relaxation) for an equal amount of time. Examining effects of these adjunctive interventions was outside the scope of the present study, but exploratory analyses indicated there were no substantive differences in any outcomes of interest for exercise versus healthy living subgroups, so primary analyses proceeded using the planned strategy of relying on a combined SZ sample.

HC participants were recruited from the greater Los Angeles community and screened to match the demographic composition of the patient sample in terms of age, gender, race/ethnicity, and estimated socioeconomic status (measured using highest level of parental education as a proxy). Subsequent screening for eligibility was conducted using the SCID-5-RV (First et al., 2015). Prospective HC participants were excluded if they had a history of any schizophrenia spectrum or other psychotic disorders, current or recurrent major depressive episodes, bipolar

disorders, obsessive-compulsive disorder, post-traumatic stress disorder, attention-deficit/hyperactivity disorder, neurological disorders, alcohol/substance use disorder, or significant head injury involving loss of consciousness; if they had any first-degree relatives with a psychotic disorder; or if they were pregnant or lactating.

Study Design

All participants underwent cognitive testing and EEG data collection upon enrollment in the study ("baseline") and again approximately six months later. During the six-month period between study visits, SZ participants completed a computerized CT intervention as part of their outpatient treatment program. HC participants did not undergo any intervention or receive any study-related contact between visits.

All procedures were approved by the UCLA Institutional Review Board. All participants provided written informed consent before participating and were debriefed and compensated at the conclusion of each study visit. Participants were instructed to refrain from using drugs or alcohol within 24 hours prior to the EEG session and to refrain from smoking cigarettes or consuming caffeine at least one hour prior to data acquisition.

Cognitive Assessment

For all participants, cognitive functioning was assessed using the MATRICS Consensus Cognitive Battery (MCCB; Nuechterlein et al., 2008), a standardized test suite that measures seven cognitive domains relevant to schizophrenia: attention/vigilance, speed of processing, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition; as well as an overall composite representing general cognitive functioning. Raw subscale and composite scores were converted to age- and gender-adjusted T-scores. The MCCB has been shown to have excellent reliability and validity in relevant samples and provides

demographically-representative normative data stratified by age, gender, and education (Kern et al., 2008; Nuechterlein et al., 2008). All tests were administered under standardized conditions by trained personnel. For the present study, only the attention/vigilance, speed of processing, working memory, and composite scores were included in analyses.

For SZ participants, attentional functioning was further assessed using the inattention subscale of the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983). The SANS is a clinician-rated measurement of negative symptom severity with 25 items across 5 subscales: affective flattening, alogia, avolition-apathy, anhedonia-asociality, and inattention. Each item is rated on a scale from 0 (not at all) to 5 (severe), with evidence of good interrater reliability (Moscarelli et al., 1987). Prior research has demonstrated a consistent relationship between SANS-rated inattention and P50 ratio scores (Hamilton et al., 2018; Yee et al., 1998).

Cognitive Training Intervention

Between study visits, SZ participants completed a Posit Science CT program at the UCLA Aftercare Research Program. Training took place 2 days per week, with 2 separate 1-hour sessions per day (4 hours per week total) for 6 months. The first half of the intervention involved neurocognitive training (BrainHQ) with a focus on auditory discrimination, processing speed, working memory, verbal memory, and verbal reasoning. The second half of the intervention involved social cognitive training (SocialVille) with a focus on face recognition, emotion identification, and interpretation of social cues. Training started with relatively basic processes and progressed to more complex processes, with difficulty level increasing within processes and adapting to the individual patient's performance. Computerized activities were presented in an engaging game-like format with additional reinforcement built in (e.g., earning stars and completing levels) to enhance participation and motivation. Training was completed

independently in a group computer lab setting with monitoring and as-needed assistance (e.g., suggesting cognitive strategies to use to improve performance) from a cognitive coach.

Paired-Stimulus Procedure

EEG data were collected as participants sat comfortably in front of a computer monitor in a sound-attenuated room and listened to 160 trials of paired auditory stimuli at 76 dB sound pressure level that were presented via bilateral foam-insert earphones. Participants underwent audiometric screening beforehand to ensure normal levels of hearing. Each stimulus (2 per trial, 320 total) was 3 ms in duration, and there was a 500 ms interstimulus interval between stimuli within a trial. There was a variable 9-11 s interval between trials, with 32 trials per block and short breaks between the 5 blocks.

Participants were instructed to sit quietly and passively listen to a series of tones. A black background with a white cross was displayed on the computer monitor as an optional visual fixation point to minimize eye movement.

EEG Recording

EEG data were recorded from 96 scalp electrodes at a sampling rate of 2000 Hz using a Brain Products actiCHamp amplifier and actiCAP active electrode system (Classic model for the first 25 participants, all SZ; Slim model #BP-135-1500 for the remaining 49 SZ and 41 HC participants) and Brain Products electrode caps appropriate to each participant's head size (Classic style for the first 25 SZ; SnapCap model #AS-096-C-U-HP-W for all remaining participants). Electrodes were referenced to the left mastoid at recording. The 96 electrodes included sensors placed above, below, and adjacent to the external canthus of each eye, providing vertical and horizontal electrooculogram (EOG) channels. Impedances were minimized at each electrode, typically below 25 kΩ per vendor guidance. A Brain Products

StimTrak adapter was used to time-lock the auditory stimulus presentation during recording to the ERP during analyses. Three-dimensional coordinates of electrode positions were recorded using a Brain Products CapTrak spatial digitizer, with fiducial landmarks on the nasion and preauricular points to aid in spatial reconstruction during data processing.

EEG Data Processing and Analysis

EEG data were processed and analyzed using EEGLAB (version 2023.0; Delorme & Makeig, 2004) and ERPLAB (version 8.20; Lopez-Calderon & Luck, 2014) toolboxes in MATLAB (version R2023b; The MathWorks Inc., 2023). Data were re-referenced to the average mastoids linked offline using a linear derivation (Miller et al., 1991). Continuous EEG data underwent preliminary visual quality inspection by a team of trained staff to identify periods in the data with oculomotor or myogenic artifacts. Channels contributing significant and untreatable noise (e.g., due to disconnection or high impedance) were removed from the montage. Residual line noise was filtered from all channels using a 60 Hz notch filter.

Independent component analysis (ICA) was conducted using the Extended Infomax algorithm, and components associated with eye movement, blink artifact, and electrocardiographic activity were flagged by a team of trained staff blind to group membership (SZ, HC) and study visit (baseline, six-month). EEG data were then reconstructed without the flagged components, downsampled to 1000 Hz, and filtered separately for P50 and N100. Previous studies have demonstrated the acceptability of analyzing P50 and N100 within the same trial-averaged data, using both overlapping (Shen et al., 2020) and non-overlapping (A. K. Smith et al., 2010) filter parameters, with no evidence of the neighboring component interfering with the identification and scoring of the target component. Filtered data were epoched into -200 to +1000 ms trials relative to S1 onset and subtracted from the average of the 200 ms pre-S1

baseline. Epoched data were screened for additional artifact at Cz using a voltage range threshold of ±100 μV within a trial, with trials exceeding these thresholds excluded from further processing.

P50 Processing and Scoring

Continuous ICA-reconstructed EEG data were filtered using a 10 to 50 Hz bandpass finite-impulse response filter (1321 weights, 660 per side). Filtered data were epoched into trials, with a minimum of 94 usable trials required to be included in P50 analyses. This number was chosen after systematic evaluation to maximize signal-to-noise ratio and sample size and to minimize potential influence of fatigue on P50. A participant's first 94 artifact-free trials were averaged to yield mean waveforms for each scalp channel.

P30, N40, and P50 ERP components were scored at the Cz channel and automatically identified using the findpeaks function in MATLAB. P30 was identified as the maximum positive peak 20-40 ms post-stimulus presentation and was used to identify N40. N40 was identified as the maximum negative peak between P30 and P50 and was used to score P50, the target component. P50 was identified as the maximum positive peak 40-80 ms post-stimulus presentation. Using peak-to-peak scoring, P50 amplitude was scored relative to N40 amplitude (i.e., P50 minus N40), in μV. This scoring process was completed separately for S1 and S2. Identified peaks were manually reviewed by a team of graduate student raters (blind to group membership and study visit) to confirm that identified components met all aforementioned requirements. Discrepancies were flagged for consensus review by the principal investigator (also blind to group membership and study visit), with as-needed consultation of neighboring channels and components (e.g., P70 at Fz and Pz) to assist with P50 identification at Cz.

The P50 gating ratio score was computed as P50 amplitude to S2 divided by P50 amplitude to S1. In the absence of a discernable P50 peak in response to S2, S2 P50 was scored as having essentially zero amplitude (0.001 μV) and interpreted as reflecting complete suppression. The upper limit of P50 ratio scores was truncated to 2.00 (for n = 4 SZ at baseline, n = 1 SZ at follow-up, and n = 1 HC at follow-up) to prevent outliers from having a disproportionate effect on group means, consistent with recommendations in the literature (e.g., Nagamoto et al., 1991). Therefore, P50 ratio scores ranged from 0.00 (complete suppression) to 2.00 (100% augmentation).

N100 Processing and Scoring

Continuous ICA-reconstructed EEG data were filtered using a 1 to 20 Hz bandpass finite-impulse response filter (3301 weights, 1650 per side). Due to concerns about fatigue effects on N100, which is generally more susceptible to fluctuating attention over the course of an experimental session, only the first block of 32 trials was averaged to yield mean waveforms for each scalp channel. N100 to S1 was computed as the maximum negative peak between 80 to 120 ms post-stimulus onset, with the amplitude measured relative to pre-stimulus baseline. For waveforms that did not have a 3-point peak negativity within this narrow latency window, a more liberal latency window was applied with N100 computed as the maximum negative peak between 50 to 150 ms post-stimulus onset.

Statistical Analyses

The majority of analyses were conducted in RStudio (version 2025.9.0.387; Posit team, 2025). Participants with missing or unusable data for a certain predictor or outcome were deleted pairwise to maximize statistical power across analyses. Welch's t-tests and analyses of variance (ANOVA) were used to examine group differences in baseline P50 gating ratios, P50/N100

amplitudes, and MCCB scores, as well as group-by-time interaction effects. Pearson correlations were used to examine relationships between ERP measures and domains of cognitive functioning at each timepoint. An alpha cutoff of .05 was used across analyses. No adjustment for multiple comparisons was done due to the hypotheses being individually grounded in prior literature, other than applying a two-tailed alpha threshold to the set of one-tailed hypotheses.

Multilevel growth models were estimated in Blimp Studio (version 3.2.2; Enders et al., 2023) to examine individual participants' baseline-to-follow-up changes in auditory (P50 gating ratios, P50 and N100 amplitudes) and cognitive (MCCB, SANS-Inattention) measures, and to investigate potential moderating relationships between intervention-related auditory and cognitive changes. Repeated auditory and cognitive measures were treated as Level 1 variables nested within individuals (Level 2). Study visit (baseline vs. follow-up) was converted into a continuous time variable (month, 0 or 6) and was included as a Level 1 predictor. Group (SZ vs. HC) was included as a Level 2 predictor, dummy-coded with HC as the reference group. Random intercepts and slopes for time were specified to examine longitudinal trends of interest. Models were estimated using Markov Chain Monte Carlo (MCMC) estimation with 20,000 iterations following a burn-in of 20,000; both were increased to 40,000 for models with interaction terms to improve convergence. Convergence was adequate for all models (Final PSR < 1.05, number of effective MCMC samples all > 100), and a 95% credible interval was used to evaluate statistical significance.

Results

Participants

Demographic and clinical characteristics of the two samples are presented in Table 1. The SZ and HC groups were well matched and did not significantly differ in the composition of

Table 1. Demographic and clinical characteristics of the full sample.

	SZ (N = 74)	HC (N = 41)	Statistical Comparison
Demographics	*n (%)*	*n (%)*	
Gender			
Female	25 (34%)	12 (29%)	$\chi^2(1) = 0.083$, $p = .77$
Male	49 (66%)	29 (71%)	
Ethnicity			
Hispanic/Latine	25 (34%)	15 (37%)	$\chi^2(1) = 0.0096$, $p = .92$
Not Hispanic/Latine	49 (66%)	26 (63%)	
Race			
American Indian or Alaskan Native	1 (1.3%)	2 (4.9%)	
Asian	15 (20.3%)	8 (19.5%)	
Black or African American	5 (6.8%)	4 (9.8%)	$\chi^2(4) = 3.06$, $p = .55$
White	25 (33.8%)	9 (22.0%)	
More than One Race	28 (37.8%)	18 (43.9%)	
Diagnosis			
Schizoaffective-depressed	4 (5.4%)		
Schizophrenia	60 (81.1%)	--	--
Schizophreniform	10 (13.5%)		
Demographics, continued	*M(SD)*	*M(SD)*	
Age, years	22.4 (4.8)	21.5 (3.2)	$t(113) = 1.04$, $p = .30$
Education, years	14.0 (2.0)	14.3 (1.6)	$t(113) = -0.73$, $p = .47$
Highest parental education, years	15.3 (3.5)	15.6 (4.1)	$t(113) = -0.41$, $p = .68$
Baseline cognitive functioning	*M(SD)*	*M(SD)*	
MCCB Attention/Vigilance[a]	38 (11.2)	46 (9.3)	$t(110) = -3.44$, $p = .0008$
MCCB Processing Speed[a]	34 (11.8)	51 (10.5)	$t(110) = -7.71$, $p < .0001$
MCCB Working Memory[a]	41 (13.3)	52 (10.2)	$t(110) = -4.47$, $p < .0001$
MCCB Composite[a]	32 (12.5)	49 (10.5)	$t(110) = -7.26$, $p < .0001$
SANS Inattention[b]	2.11 (1.09)	--	--

Note: MCCB, MATRICS Consensus Cognitive Battery (Nuechterlein et al., 2008); SANS, Scale for the Assessment of Negative Symptoms (Andreasen, 1989).
[a] Based on $n = 74$ SZ and $n = 38$ HC
[b] Based on $n = 65$ SZ

gender, ethnicity, or race, and did not differ in mean age, years of education, or years of parental education (used as a proxy for estimated socioeconomic status). As expected, SZ differed significantly from HC in baseline MCCB scores.

Baseline Replication of Auditory Impairments

Baseline mean ERP amplitudes and ratio scores for each group are presented in Table 2a. Consistent with hypotheses, a 2×2 Group × Stimulus repeated-measures ANOVA on P50 amplitudes revealed main effects of group, $F(1,107) = 10.11$, $p = .002$, with a smaller P50 overall for SZ than HC; and of stimulus, $F(1,107) = 98.01$, $p < .001$, with a larger P50 to S1 than S2; as well as an interaction, $F(1,107) = 4.52$, $p = .04$, which is illustrated in Figure 1. Simple-effects tests showed a medium effect of group for S1, $t(107) = 3.05$, $p = .003$, $d = 0.64$, and a small effect of group for S2, $t(107) = 2.33$, $p = .02$, $d = 0.26$. Although P50 ratio scores were in the expected direction, the group difference was not statistically significant. For N100, SZ had smaller responses to S1 than the HC group, as predicted.

Figure 1. Amplitude of P50 ERP component in response to each stimulus, by group. Error bars represent ±1 standard error of the mean.

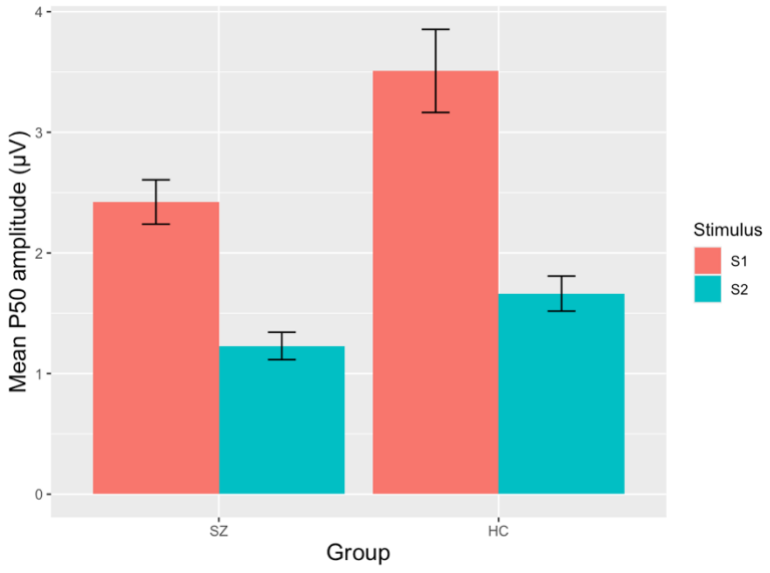


Table 2a. Baseline auditory ERP measures.

	SZ *M (SD)*	**HC** *M (SD)*	*t*-statistic	df	*p*	*d*
S1 P50, μV[a]	2.42 (1.52)	3.51 (2.18)	2.78	61.4	.007	0.61
S2 P50, μV[a]	1.23 (0.95)	1.66 (0.92)	2.35	83.5	.02	0.46
S2/S1 P50 ratio score[a]	0.62 (0.53)	0.57 (0.35)	0.62	104.6	.54	0.11
S1 N100, μV[b]	-3.92 (3.12)	-6.84 (4.26)	3.84	64.4	.0003	0.82

Table 2b. Baseline auditory-cognitive relationships.

	MCCB Attention/ Vigilance	MCCB Processing Speed	MCCB Working Memory	MCCB Composite	SANS Inattention
S1 P50, μV[a]	.19	.20*	.15	.28**	-.15
S2 P50, μV[a]	.09	.17	.11	.18	.01
S2/S1 P50 ratio score[a]	-.04	.03	-.03	-.05	.15
S1 N100, μV[b]	-.28**	-.31**	-.28**	-.36***	.07

Note: SZ and HC both included in MCCB correlations; only SZ included in SANS correlations.
** p < .05, ** p < .01, *** p < .001*
[a] *n* = 69 SZ and *n* = 40 HC
[b] *n* = 73 SZ and *n* = 41 HC

Baseline ERP-cognition correlations are presented in Table 2b. S1 P50 amplitudes showed significant correlations with MCCB processing speed and composite scales, with larger P50 amplitudes associated with stronger cognitive functioning. Larger (more negative) N100 amplitudes were also associated with better cognitive functioning across attention/vigilance, processing speed, working memory, and composite scales. No significant correlations emerged for S2 P50 or P50 ratio scores.

Longitudinal Auditory Changes

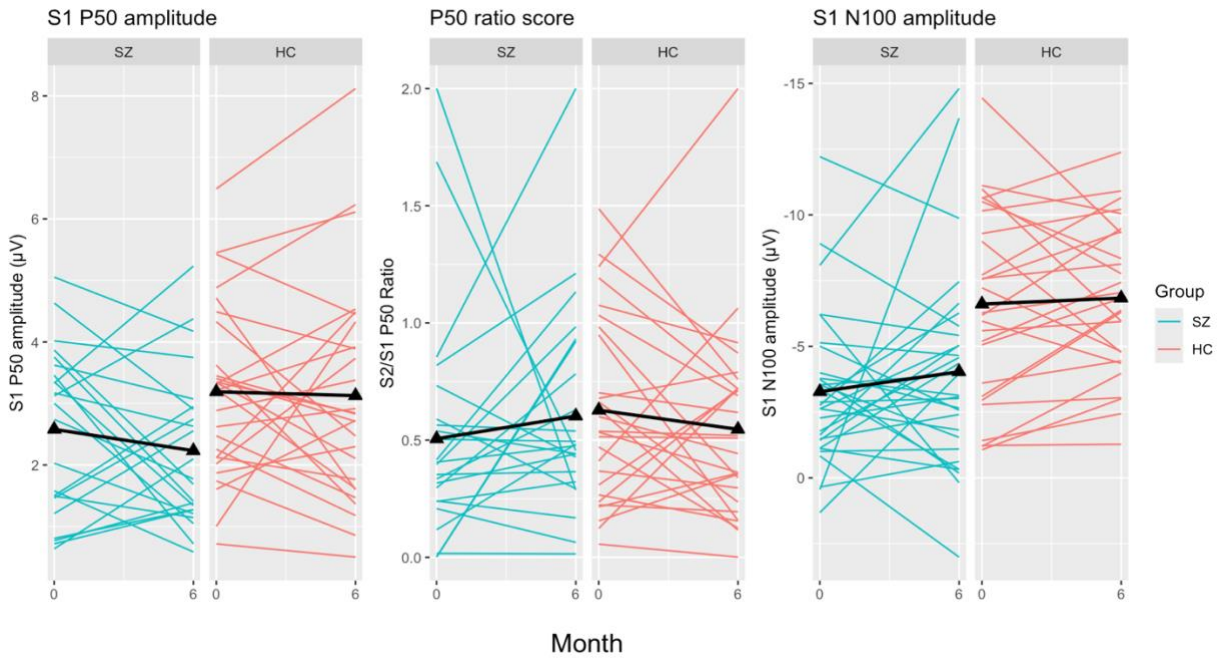
Contrary to predictions, there was no evidence of group-level reductions in P50 ratio scores or enhancements in P50 and N100 amplitudes to S1 following CT relative to baseline within the SZ group (see Table 3). Main effects of group emerged for S1 P50 and N100 amplitudes, but null main effects of study visit and lack of interaction effects do not support the proposed model of broad auditory improvements following the CT intervention in the subsamples for whom data were available. Participant-level examination of baseline-to-follow-up changes suggest considerable heterogeneity (see Figure 2), which may partially explain the absence of group-level effects and supports the planned strategy to examine factors that influence individual response trajectories.

Table 3. Longitudinal auditory ERP measures and effects.

	Baseline		**6-month follow-up**		**Group main effect**		**Interaction effect**	
	SZ *M (SD)*	**HC** *M (SD)*	**SZ** *M (SD)*	**HC** *M (SD)*	*F*	*p*	*F*	*p*
S1 P50, μV[a]	2.58 (1.34)	3.19 (1.42)	2.23 (1.26)	3.13 (1.79)	4.22	.048	0.48	.49
S2/S1 P50 ratio score[a]	.51 (.49)	.63 (.40)	.60 (44)	.55 (.41)	0.11	.74	1.42	.24
S1 N100, μV[b]	-3.28 (2.89)	-6.61 (3.66)	-4.04 (3.82)	-6.84 (2.90)	15.93	.0002	0.35	.55

Note: Baseline means presented in this table differ from those previously presented in Table 2, due to being based on different subsets of the overall sample. Values presented here represent only participants who returned for follow-up and were included in longitudinal analyses.
[a] Based on n = 23 SZ and n = 27 HC; and (1,48) degrees of freedom
[b] Based on n = 30 SZ and n = 27 HC; and (1,55) degrees of freedom

Figure 2. Changes in auditory ERP outcomes from baseline to follow-up, by group. Left: S1 P50 amplitude; Center: P50 ratio score; Right: S1 N100 amplitude (y-axis is reversed). Thin lines represent individual patient trajectories for the full longitudinal sample. Thick black lines represent group mean changes from baseline to follow-up. Triangles represent group means at each timepoint.



Relationships between Baseline Auditory Functioning and Auditory Change

Results from multilevel growth models with time as a Level 1 predictor, group as a Level 2 predictor, and auditory ERPs as outcomes for each model are summarized in Tables 4a-c. Models corroborated the null effect of time (study visit) on all ERP measures across groups. Groups differed in N100 amplitudes at baseline, with larger amplitudes for HC than for SZ, but no baseline differences in S1 P50 or P50 ratio scores were observed. Group × Month interaction effects were not significant for any of the ERP outcomes.

Contrary to hypotheses, baseline auditory ERP measures did not reliably covary with the magnitude of change in those measures over time. Thus, although individual auditory changes over time varied widely, this variability was not explained by baseline scores or group

membership, and only a small proportion (3-17%) of the variability in ERP outcomes was accounted for by these models.

To examine effects of the CT intervention, exploratory models limited to the SZ group were run (see right column of Tables 4a-c). Models yielded similar patterns of individual-level effects, with one exception. Baseline P50 ratio scores covaried negatively with slope of change in P50 ratio scores following the intervention, indicating that patients who had a larger-than-average ratio score at baseline (poorer gating) tended to have a more negative slope (greater reduction in ratio score) from pre- to post-CT. This finding should be interpreted with caution, as the overall slope of change over time was not significantly different from 0.

Tables 4a-c. Multilevel growth models of auditory outcomes. Group (dummy-coded HC/SZ) included as a Level 2 predictor and Month (0 or 6) as a continuous Level 1 predictor. All betas displayed are unstandardized. Boldface indicates an estimate with a credible interval that does not contain 0. CI = credible interval, Var = variance, Cov = covariance.

Table 4a. Estimates for multilevel growth modeling of S1 P50 amplitude

	Model 1: Full sample		**Model 2: SZ only**	
FIXED EFFECTS				
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**3.18**	**[2.62, 3.75]**	**2.57**	**[1.91, 3.24]**
Group	-0.62	[-1.44, 0.21]	--	--
Month	-0.01	[-0.11, 0.09]	-0.06	[-0.18, 0.06]
Group × Month	-0.05	[-0.20, 0.10]	--	--
RANDOM EFFECTS				
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**1.63**	**[0.70, 2.92]**	**1.71**	**[0.43, 4.32]**
Cov(Month,Intercept)	-0.06	[-0.23, 0.07]	-0.14	[-0.51, 0.04]
Var(Month)	**0.04**	**[0.01, 0.08]**	**0.04**	**[0.003, 0.13]**
Residual variance	**0.52**	**[0.02, 1.31]**	**0.62**	**[0.03, 1.74]**
PROPORTION VARIANCE EXPLAINED				
By overall model	0.07	[0.01, 0.21]	0.01	[0.00, 0.11]

Table 4b. Estimates for multilevel growth modeling of P50 ratio score

	Model 1: Full sample		**Model 2: SZ only**	
FIXED EFFECTS				
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**0.63**	**[0.45, 0.80]**	**0.5**	**[0.25, 0.74]**
Group	-0.13	[-0.39, 0.14]	--	--
Month	-0.01	[-0.05, 0.02]	0.02	[-0.04, 0.07]
Group × Month	0.03	[-0.02, 0.08]	--	--
RANDOM EFFECTS				
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**0.15**	**[0.04, 0.29]**	**0.21**	**[0.03, 0.56]**
Cov(Month,Intercept)	-0.02	[-0.04, 0.00]	**-0.03**	**[-0.10, -0.001]**
Var(Month)	**0.01**	**[0.001, 0.01]**	**0.01**	**[0.001, 0.03]**
Residual variance	**0.07**	**[0.003, 0.17]**	**0.10**	**[0.003, 0.27]**
PROPORTION VARIANCE EXPLAINED				
By overall model	0.03	[0.003, 0.11]	0.02	[0.00, 0.13]

Table 4c. Estimates for multilevel growth modeling of S1 N100 amplitude

Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**-6.61**	**[-7.92, -5.26]**	**-3.29**	**[-4.46, -2.09]**
Group	**3.34**	**[1.48, 5.16]**	--	--
Month	-0.04	[-0.27, 0.20]	-0.13	[-0.41, 0.15]
Group × Month	-0.09	[-0.42, 0.23]	--	--
RANDOM EFFECTS				
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**8.63**	**[3.69, 15.30]**	**6.77**	**[1.21, 15.64]**
Cov(Month,Intercept)	-0.42	[-1.33, 0.21]	-0.42	[-1.85, 0.51]
Var(Month)	**0.17**	**[0.02, 0.41]**	**0.35**	**[0.07, 0.82]**
Residual variance	**3.35**	**[0.27, 7.30]**	**3.47**	**[0.18, 10.18]**
PROPORTION VARIANCE EXPLAINED				
By overall model	0.17	[0.05, 0.32]	0.01	[0.00, 0.10]

Relationships between Auditory Change and Cognitive Change

Multilevel growth models predicting cognitive outcomes as a function of time (Level 1), ERP measures (Level 1), and group membership (Level 2) were run on each auditory-cognitive pairing. Models did not yield any substantive findings in support of the hypothesized relationships between auditory and cognitive change trajectories. Although meaningful

variability in cognitive trajectories was present across individuals, significant variability remained after accounting for ERP measures, and there was no evidence that within-person changes in S1 P50 or N100 amplitude or P50 ratio scores were associated with changes in cognitive outcomes over time. Model estimates are summarized in Tables 5a-e. The same pattern of results was observed in exploratory models including the SZ group only.

Tables 5a-e. Multilevel growth models of cognitive outcomes. Group (dummy-coded HC/SZ) included as a Level 2 predictor, Month (0 or 6) as a continuous Level 1 predictor, and ERP predictors partitioned into Level 1 variability (ERP_w = within-person) around a latent Level 2 person-specific mean (ERP_b = between-person). Models in Table 5e predicting SANS Inattention include SZ only and do not include Group predictors or interaction terms. All betas displayed are unstandardized. Boldface indicates an estimate with a credible interval that does not contain 0.

Table 5a. Estimates for multilevel growth modeling of MCCB Processing Speed

	Model 1: Predicted by S1 P50 Amplitude		**Model 2: Predicted by P50 Ratio**		**Model 3: Predicted by S1 N100 Amplitude**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**50.66**	**[46.02, 55.31]**	**51.4**	**[47.07, 55.98]**	**49.74**	**[43.81, 55.32]**
Group	**-17.74**	**[-24.16, -10.81]**	**-19.58**	**[-26.16, -13.19]**	**-14.87**	**[-23.30, -5.64]**
ERP_w	0	[-3.25, 3.41]	1.22	[-7.35, 9.81]	0.22	[-1.00, 1.43]
ERP_b	1.87	[-1.23, 5.66]	-9.07	[-23.75, 4.01]	-1.01	[-3.08, 0.74]
Month	**0.7**	**[0.11, 1.29]**	**0.72**	**[0.14, 1.30]**	**0.74**	**[0.16, 1.29]**
Group × Month	-0.27	[-1.12, 0.6]	-0.27	[-1.13, 0.61]	-0.25	[-1.02, 0.52]
ERP_w × Month	-0.14	[-0.94, 0.57]	-0.51	[-2.67, 1.63]	-0.07	[-0.37, 0.23]
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**100.26**	**[53.97, 169.88]**	**95.57**	**[49.15, 166.44]**	**131.8**	**[79.11, 212.87]**
Cov(Month,Intercept)	**-7.00**	**[-15.04, -0.97]**	**-6.56**	**[-14.49, -1.25]**	**-7.42**	**[-15.07, -1.83]**
Var(Month)	**1.24**	**[0.15, 2.72]**	**1.15**	**[0.17, 2.60]**	**1.07**	**[0.18, 2.34]**
Residual variance	**15.17**	**[0.62, 41.11]**	**15.89**	**[0.94, 39.18]**	**15.28**	**[1.60, 36.39]**
PROPORTION VARIANCE EXPLAINED						
By overall model	0.54	[0.37, 0.67]	0.56	[0.38, 0.70]	0.45	[0.28, 0.6]

Table 5b. Estimates for multilevel growth modeling of MCCB Working Memory

	Model 1: Predicted by S1 P50 Amplitude		**Model 2: Predicted by P50 Ratio**		**Model 3: Predicted by S1 N100 Amplitude**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**50.89**	**[45.69, 55.73]**	**51.62**	**[46.95, 56.35]**	**50.92**	**[44.48, 56.76]**
Group	**-12.12**	**[-20.88, -3.83]**	**-14.03**	**[-20.9, -7.33]**	**-10.99**	**[-20.14, -1.58]**
ERP_w	-0.60	[-3.89, 2.43]	-3.9	[-12.49, 3.95]	-0.68	[-1.97, 0.61]
ERP_b	2.05	[-2.37, 6.65]	-4.46	[-21.26, 12.97]	-0.49	[-2.72, 1.40]
Month	0.48	[-0.09, 1.04]	0.48	[-0.09, 1.05]	0.46	[-0.13, 1.04]
Group × Month	0.20	[-0.62, 1.03]	0.18	[-0.64, 1.03]	0.18	[-0.62, 0.98]
ERP_w × Month	0.26	[-0.50, 1.12]	1.43	[-0.75, 3.89]	0.14	[-0.18, 0.47]
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**128.51**	**[72.25, 217.82]**	**130.81**	**[76.02, 216.5]**	**167.98**	**[104.93, 267.26]**
Cov(Month,Intercept)	-3.34	[-10.54, 2.4]	-3.23	[-10.43, 2.57]	**-7.43**	**[-16.02, -1.05]**
Var(Month)	**1.00**	**[0.09, 2.35]**	**0.97**	**[0.10, 2.31]**	**1.19**	**[0.12, 2.65]**
Residual variance	**15.09**	**[0.88, 39.94]**	**14.13**	**[0.53, 37.99]**	**16.64**	**[0.9, 41.79]**
PROPORTION VARIANCE EXPLAINED						
By overall model	0.30	[0.13, 0.47]	0.28	[0.12, 0.46]	0.23	[0.09, 0.40]

Table 5c. Estimates for multilevel growth modeling of MCCB Attention/Vigilance

	Model 1: Predicted by S1 P50 Amplitude		**Model 2: Predicted by P50 Ratio**		**Model 3: Predicted by S1 N100 Amplitude**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**45.66**	**[41.49, 49.58]**	**46.04**	**[42.19, 49.89]**	**44.85**	**[39.69, 49.81]**
Group	**-9.04**	**[-15.48, -3.24]**	**-9.62**	**[-15.49, -3.89]**	**-6.90**	**[-14.41, 1.36]**
ERP_w	0.18	[-3.06, 2.84]	2.19	[-4.02, 8.48]	0.00	[-1.03, 1.12]
ERP_b	0.49	[-3.18, 4.18]	-12.54	[-28.43, 0.77]	-0.74	[-2.67, 0.88]
Month	0.21	[-0.32, 0.75]	0.24	[-0.27, 0.74]	0.17	[-0.39, 0.72]
Group × Month	0.27	[-0.48, 1.03]	0.17	[-0.56, 0.90]	0.19	[-0.54, 0.95]
ERP_w × Month	-0.01	[-0.78, 0.91]	0.74	[-1.14, 2.62]	-0.06	[-0.36, 0.21]
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**82.13**	**[45.33, 137.79]**	**67.47**	**[25.08, 122.17]**	**100.86**	**[56.51, 166.84]**
Cov(Month,Intercept)	-0.14	[-5.35, 4.15]	-0.41	[-5.34, 3.61]	-3.26	[-9.57, 1.71]
Var(Month)	**0.88**	**[0.12, 2.05]**	**0.71**	**[0.09, 1.77]**	**0.93**	**[0.07, 2.21]**
Residual variance	**12.84**	**[0.36, 32.64]**	**12.66**	**[0.98, 29.92]**	**15.57**	**[0.69, 38.39]**
PROPORTION VARIANCE EXPLAINED						
By overall model	0.19	[0.06, 0.36]	0.31	[0.11, 0.58]	0.19	[0.06, 0.37]

Table 5d. Estimates for multilevel growth modeling of MCCB Composite

	Model 1: Predicted by S1 P50 Amplitude		**Model 2: Predicted by P50 Ratio**		**Model 3: Predicted by S1 N100 Amplitude**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**48.12**	**[44.04, 52.32]**	**49.32**	**[45.35, 53.47]**	**46.12**	**[38.64, 51.58]**
Group	**-18.65**	**[-24.84, -12.15]**	**-20.95**	**[-27.18, -15.33]**	**-13.28**	**[-21.82, -0.93]**
ERP_w	1.35	[-1.03, 3.65]	-0.70	[-7.37, 5.61]	-0.10	[-1.10, 0.82]
ERP_b	2.65	[-0.68, 6.15]	**-14.61**	**[-29.26, -1.54]**	**-1.74**	**[-5.4, -0.05]**
Month	**0.82**	**[0.40, 1.25]**	**0.79**	**[0.36, 1.23]**	**0.79**	**[0.36, 1.21]**
Group × Month	0.05	[-0.55, 0.65]	0.02	[-0.62, 0.65]	-0.09	[-0.68, 0.5]
ERP_w × Month	-0.14	[-0.74, 0.48]	0.22	[-1.53, 2.15]	-0.02	[-0.27, 0.23]
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**87.96**	**[52.78, 146.88]**	**80.44**	**[41.74, 138.73]**	**129.54**	**[73.72, 207.78]**
Cov(Month,Intercept)	-1.80	[-6.31, 1.87]	-2.45	[-7.38, 1.30]	**-5.15**	**[-10.60, -1.15]**
Var(Month)	**0.50**	**[0.04, 1.27]**	**0.61**	**[0.06, 1.42]**	**0.66**	**[0.10, 1.43]**
Residual variance	**9.62**	**[0.52, 22.89]**	**9.03**	**[0.31, 23.58]**	**8.37**	**[0.25, 21.63]**
PROPORTION VARIANCE EXPLAINED						
By overall model	0.56	[0.39, 0.69]	0.61	[0.42, 0.75]	0.50	[0.31, 0.70]

Table 5e. Estimates for multilevel growth modeling of SANS Inattention

	Model 1: Predicted by S1 P50 Amplitude		**Model 2: Predicted by P50 Ratio**		**Model 3: Predicted by S1 N100 Amplitude**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**2.06**	**[1.47, 2.65]**	**2.04**	**[1.43, 2.62]**	**2.15**	**[1.66, 2.64]**
ERP_w	-0.11	[-0.69, 0.45]	0.02	[-1.45, 1.49]	0.05	[-0.14, 0.23]
ERP_b	-0.48	[-1.71, 0.51]	0.62	[-1.95, 3.10]	0.09	[-1.17, 1.51]
Month	**-0.14**	**[-0.25, -0.03]**	**-0.14**	**[-0.24, -0.03]**	**-0.15**	**[-0.25, -0.06]**
ERP_w × Month	0.03	[-0.10, 0.17]	-0.07	[-0.46, 0.32]	0.00	[-0.03, 0.04]
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**1.03**	**[0.18, 2.80]**	**1.17**	**[0.22, 3.14]**	**0.89**	**[0.14, 2.25]**
Cov(Month,Intercept)	-0.10	[-0.35, 0.03]	-0.10	[-0.36, 0.04]	-0.09	[-0.30, 0.03]
Var(Month)	0.03	[0.00, 0.09]	0.03	[0.00, 0.09]	0.03	[0.00, 0.08]
Residual variance	**0.37**	**[0.02, 1.20]**	**0.42**	**[0.02, 1.21]**	**0.45**	**[0.03, 1.18]**
PROPORTION VARIANCE EXPLAINED						
By overall model	0.23	[0.06, 0.56]	0.20	[0.05, 0.47]	0.24	[0.08, 0.52]

Discussion

Study 1 sought to build on prior work examining auditory and cognitive impairments in schizophrenia by replicating baseline relationships in a first-episode sample and investigating whether an intervention targeting cognitive impairments could reliably foster changes in auditory impairments, providing support for a mechanistic relationship of impairment and improvement between early auditory processing and higher-order cognitive functioning. It was hypothesized that the CT intervention would lead to improvements in early auditory processing, as measured by ERP measures that index stimulus registration (S1 P50 and N100 amplitude) and filtering (P50 ratio score), but that these changes would be dependent on a patient's level of baseline impairment which, in turn, would influence the magnitude of cognitive gains from CT.

Results of the present study provided partial replication of the literature on auditory processing impairments in schizophrenia. P50 and N100 amplitudes to S1 were smaller in SZ than in HC, which is consistent with findings from numerous studies and meta-analyses examining responses to the first stimulus in the pair (Brenner et al., 2009; Z. Lu et al., 2025; Patterson et al., 2008; Rosburg et al., 2008; A. K. Smith et al., 2010). Smaller ERP amplitudes to S1 can be taken as support for a reduction in the extent to which a novel stimulus is initially registered in schizophrenia, which would limit the information that can be attended to and integrated, thereby contributing to interruptions in subsequent functions (Adcock et al., 2009; Marchi, 2020). Accordingly, responses to S1 were significantly associated with general cognitive functioning as reflected by the MCCB composite score (P50 and N100) as well as speed of processing (P50 and N100), attention/vigilance (N100), and working memory (N100), with a smaller response associated with poorer cognitive performance across both SZ and HC groups.

Models of sensory gating typically propose that initial stimulus registration is the trigger that initiates the inhibitory cascade resulting in the suppressed response to the second stimulus (Freedman et al., 1987). However, there is much debate regarding whether P50 sensory gating impairments in schizophrenia primarily reflect a reduced response to S1 or an amplified (or not sufficiently suppressed) response to S2 (Brenner et al., 2009; W.-P. Chang et al., 2011; Patterson et al., 2008; A. K. Smith et al., 2010). In the present study, the SZ group showed significantly smaller P50 responses to both stimuli, with a statistical interaction indicating that this was primarily carried by S1. Poorer registration or encoding of S1 in schizophrenia could contribute to the between-groups effect observed for S1, and reduced suppression of encoding of S2 in schizophrenia could contribute to the between-groups effect observed for S2. Therefore, the present results provide plausible support for a combined model of sensory gating impairment in schizophrenia that involves both a poorer registration of S1 and less suppression of S2.

Despite these findings in support of impairment in both registration and suppression, results of this study failed to replicate group differences in P50 ratio scores at baseline, which is a key operationalization of sensory gating impairments in schizophrenia and a robust finding in the literature (Bramon et al., 2004; Heinrichs, 2004; Patterson et al., 2008), nor any relationships between P50 ratio and cognitive functioning that have been demonstrated previously (Hamilton et al., 2018; A. K. Smith et al., 2010; Thoma et al., 2003; Yee et al., 1998). The lack of group difference in baseline P50 gating ratios may reflect unusual patterns within the HC group rather than the absence of a well-documented impairment within the SZ group. The SZ group's baseline mean ratio score of 0.62 was within the range of what many of the reviewed studies have interpreted as a gating impairment (approximately 0.51 to 0.63, reported in a meta-analysis by Patterson et al., 2008), whereas the HC group's mean ratio score of 0.57 is much larger than most

studies report in healthy samples (typically approximately 0.38, from the same meta-analysis). This pattern of results is consistent with those of other studies that have found evidence of abnormal gating in healthy comparison samples that leads to an absence of group-level effects when contrasted with a schizophrenia sample that did ostensibly demonstrate impairments based on benchmarks from the literature (Brenner et al., 2009; Kathmann & Engel, 1990).

At the individual level, within the SZ group, there was evidence of a negative relationship between a patient's baseline P50 ratio score and the trajectory of their P50 ratio change following CT. Individuals with poorer gating (higher ratio scores) at baseline showed more improvement (greater reduction in ratio score), despite little overall evidence of systematic change at the group level. Prior studies have found evidence of changes in ERP markers of early auditory processing with function-specific CT (Medalia et al., 2019; Popov et al., 2011, 2015), suggesting that the broad CT used in the present study sufficiently targeted and improved certain aspects of bottom-up auditory processing. At the group level, however, present results failed to demonstrate differential changes in auditory ERPs as a result of CT. Models revealed considerable heterogeneity in participants' individual change trajectories for all auditory ERPs, as depicted in Figure 2. The heterogeneity in slopes between individuals within a group exceeded the amount of between-group variability that was observed, making it difficult to draw conclusions about systematic group differences in auditory changes despite SZ receiving an intervention and HC receiving no intervention. It is therefore difficult to draw firm conclusions about whether the intervention reliably induced changes in P50 ratio scores among individuals with schizophrenia with impaired baseline gating. Further, the variability in individual-level auditory changes over time did not reliably predict changes in cognitive functioning from baseline to follow-up, a

finding that converges with other studies examining correlations between auditory and cognitive changes (Popov et al., 2011, 2015) that found cognitive improvements to be fairly narrow.

Thus, although the present sample demonstrated significant relationships between auditory and cognitive functioning at baseline, and individuals showed substantial variability in changes in both outcomes, significant variability in cognitive trajectories remained after accounting for auditory ERPs and group membership. As discussed above, patients with schizophrenia do not show a uniform response to CT interventions, with some individuals showing dramatic improvements and others showing little or none (Vinogradov et al., 2012). The results of the present study do not support changes in ERP-based measures of early auditory processing as a central factor to explain the heterogeneity in CT-induced cognitive changes, in part because it remains unclear whether the intervention utilized with this sample reliably facilitated changes in auditory processing.

It is worth acknowledging that these data were drawn from a clinical trial examining the effects of aerobic exercise on cognitive functioning in schizophrenia, and the full scope of interventions differed for half of the patient sample; all patients completed CT, but a subset additionally trained in aerobic exercise. While this approach differs from those taken in prior studies cited, it is unlikely to have been a primary driver of null effects in the present study. On average, patients' auditory change trajectories were not reliably different depending on the type of additional intervention received, suggesting that there are other factors influencing heterogeneous responses to CT.

In sum, understanding factors that may attenuate the effects of CT in order to be able to adapt and prevent treatment non-response remains a research priority. Although the present study did not support the prediction of CT driving auditory changes, which in turn contributed to

cognitive changes, further exploration of this hypothesized model is warranted. It is possible that factors not examined in these analyses influence auditory processing impairments and improvements, thereby obscuring potential relationships that may exist with cognition. The mixed findings of Study 1 lay the foundation for further probing of these relationships in Studies 2 and 3 to understand potential factors that may moderate relationships between auditory and cognitive impairment and improvement in schizophrenia.

Study 2: Auditory Hallucinations as a Potential Moderator of Intervention-Related Changes in Early Auditory Processing

A central question in the conceptualization and treatment of schizophrenia is how symptom domains associated with the illness may be phenomenologically distinct and yet related to one another (Buchanan & Carpenter, 1994). Further contributing to the complexity, decades of research underscore marked heterogeneity both within and between individuals with schizophrenia, as supported by vast literatures identifying genetic markers, neural networks, peripheral physiological mechanisms, and psychological processes that overlap and interact to produce the array of clinical, cognitive, and behavioral symptoms that characterize the illness. Understanding the implications of overlapping and interacting mechanisms of dysfunction may be critical in assisting with treatment planning, as improvements in symptoms addressed by a specific intervention may be limited by a lack of improvement in seemingly distinct symptoms due to common component processes. Study 2 examined whether such a relationship exists between early auditory processing impairments and auditory hallucinations, wherein the latter could limit the extent to which an intervention such as CT would be able to adequately target and improve the former, due to an overlapping and interacting mechanism of disrupted auditory salience processing.

Aberrant Salience in Schizophrenia

In schizophrenia, internal and external experiences are sometimes represented in the brain as more important or significant than is typical in healthy individuals, resulting in heightened processing of the information (Kapur, 2003) and referred to at times as “hypersalience.” More recently, theoretical models of schizophrenia have examined the potential role of “hyposalience,” which involves novel or strange information receiving less processing than would be optimal (Sass & Byrom, 2015). In combination, these contrasting forms of aberrant salience have been

proposed to give rise to positive symptoms of schizophrenia, namely delusions and hallucinations (Kapur, 2003; Mallikarjun et al., 2018; Miyata, 2019; Palaniyappan & Liddle, 2012).

Neuroimaging studies have identified a salience network that spans multiple structures (e.g., anterior insula, dorsal anterior cingulate cortex) and facilitates the integration of sensory, emotional, and cognitive information (Menon, 2015; Menon & Uddin, 2010). In an early model, Kapur (2003) conceptualized the pathophysiology of aberrant salience in psychosis within motivational and reward systems in an effort to link delusions and hallucinations with emerging data on dopaminergic hyperactivity. However, there is growing evidence that positive symptoms are also associated with disruptions in salience network functioning (Mallikarjun et al., 2018; Palaniyappan & Liddle, 2012; Schiwy et al., 2022). Accordingly, aberrant salience in schizophrenia can encompass several dimensions, including motivational salience, novelty or surprise salience, and physical or featural salience (Miyata, 2019). Salience processing is closely related to attentional processing, with salience detection playing a key role in determining what information is selected for attentional resource allocation and higher-level processing (Menon, 2015). Despite some overlap, salience processing and attention are distinct processes that involve different computational and biological mechanisms (Parr & Friston, 2019).

Auditory Salience Processing

In order to attend to potentially relevant sounds in the environment without experiencing sensory overload, the auditory system must detect and select certain stimuli for further processing while limiting the processing of less relevant information. Broadly, salient stimuli are more likely to be detected, but this detection can be shaped both involuntarily (e.g., by stimulus features such as loudness, frequency, novelty) and voluntarily (e.g., as a function of the listener's

goals), which together determine whether and to what extent a given sound is salient in the immediate context (C. Kayser et al., 2005). The potential for interplay involving sensory inputs suggests that salience processing can be considered an early perceptual process that is neither fully bottom-up (i.e., involuntary) nor top-down (i.e., voluntary) (Tordini et al., 2013; White & Yee, 1997; Yee et al., 2010) but is a critical step nonetheless in determining what information gets access to the brain's finite attentional resources (Menon & Uddin, 2010).

Salience processing can be measured with electrophysiology by using the paired-stimulus gating paradigm to elicit P50 and N100 event-related brain potential (ERP) components, which are considered manifestations of different stages of salience and information processing mechanisms (Boutros et al., 2004). In response to the first stimulus in a pair, the P50 component (which is generally understood to be an early, automatic response) can be conceptualized as indexing a stimulus detection process that initiates salience processing, whereas the N100 component (which reflects largely voluntary allocation of attention) can be viewed as indexing a stimulus selection process that signifies the attribution of salience. For the second stimulus in the pair, suppression of the P50 component is attributed to detection without attribution of salience, given its repetitive nature and minimal novelty or significance. Stated differently, responses to S1 correspond to an ability to "gate in" salient information, and responses to S2 correspond to an ability to "gate out" non-salient information (Brenner et al., 2009). Together, the processes of salience detection and attribution support the capacity for sensory gating and, in turn, facilitate the filtering of auditory information.

Aberrant Auditory Salience as a Shared Mechanism Across Domains

Aberrant auditory salience processing may involve a shared mechanism that contributes to early auditory information processing impairments that are typically associated with the

cognitive symptom domain, as well as with auditory hallucinations that are a key element within the positive symptom domain. Insufficient engagement of salience processing mechanisms in response to a novel stimulus could manifest as a failure to fully detect new information, reflected in a smaller P50 amplitude to S1. A consequence is novel information would not be selected for further processing, as reflected in a smaller N100 response to S1. Lower salience assigned to S1 would then be followed by a failure to detect redundancy when the same stimulus is repeated, resulting in over-attribution of salience to S2 and a larger-than-typical P50 amplitude to S2. The S1 and S2 P50 responses can be represented together in the P50 ratio score (S2/S1), which reflects whether a response to the redundant stimulus is appropriately suppressed. A larger P50 ratio score is expected when too much salience is attributed.

Aberrant engagement of salience processing mechanisms could also contribute to the experience of auditory hallucinations. Specifically, over-attribution of salience to internal events, such as verbal thought streams, may reflect a failure to detect the self-generated origins of such signals (Ford & Mathalon, 2004, 2005) and lead to higher salience and higher processing. A specific pattern of ERP responses indexing this process is less straightforward than described above, as thoughts and hallucinations are generally not associated with detectable ERPs. Using a symptom capture procedure, Thoma et al. (2017) found larger P50 ratio scores (i.e., poorer sensory gating) while patients with chronic schizophrenia were actively hallucinating than when they were not experiencing hallucinations, consistent with a pattern of under-attribution of salience to S1 and/or over-attribution of salience to S2. The investigators also reported a trending effect such that N100 amplitude to S1 was reduced during hallucinations, consistent with a failure to detect and select the novel external stimulus as described above. Positive symptoms assessed with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) have also

been associated with more attention to nonpredictive cues during a learning task (Morris et al., 2013), again consistent with insufficient inhibitory processing of non-salient information. In a meta-analysis of voxel-based morphometry studies, Palaniyappan et al. (2012) showed that auditory hallucinations were associated with structural changes in the left insula and right superior temporal gyrus, key sites involved in salience and auditory processing, respectively. The superior temporal gyrus has also been implicated in auditory sensory gating impairments (Edgar et al., 2003; Popov et al., 2021; Williams et al., 2011).

First-person accounts from individuals with schizophrenia support the notion of a shared mechanism of aberrant auditory salience, as changes in auditory hearing and auditory perception are commonly reported as preceding or co-occurring with overt auditory hallucinations. Additionally, reports of emergence of psychotic symptoms often mention sounds producing a newfound "keenness", hyperawareness of sounds, and more intense sensory experiences, which result in heightened distractibility (Bowers & Freedman, 1966; Saks, 2007). These subjective descriptions of heightened salience of incoming auditory information are further supported by data obtained from a sample of outpatients with schizophrenia showing an association between PANSS-rated hallucination severity and sharpening of senses as assessed by a self-report inventory of psychosis proneness (Pugliese et al., 2022).

Auditory ERP components: Trait versus State Measurements

A related consideration when examining a potential shared mechanism of aberrant auditory salience processing that links early auditory information processing impairments and auditory hallucinations is the extent to which measures of auditory information processing represent stable, trait-like phenomena or are subject to changes in clinical or psychological state. As reviewed in Study 1, much research has been done to examine whether early auditory

processing impairments can be mitigated by CT interventions (e.g., Medalia et al., 2019; Popov et al., 2011, 2015). This line of research (Study 1 included) assumes to some degree that the intervention is the key driver of any changes in auditory measurements observed from pre-CT baseline to post-CT follow-up, such that the ERP components at each time point represent stable, reliable, trait-like markers. Indeed, P50 suppression impairments and abnormal N100 amplitudes have been proposed as biomarkers or endophenotypes of schizophrenia (Dondé et al., 2023; Freedman et al., 2003; Javitt & Freedman, 2015; Miller & Rockstroh, 2013, 2016; Patterson et al., 2008; Turetsky et al., 2007, 2008), reflecting their assumed reliability, which has been demonstrated for magnetic analogs (B. Y. Lu et al., 2007) but long-debated for electrical components (D. A. Smith et al., 1994).

Although they may be compelling candidates, P50 and N100 do not consistently meet all the criteria associated with invariant traits, particularly regarding whether or not they are truly state-independent -- a criterion that has been debated (for a review, see Miller & Rockstroh, 2013). The potential for state dependence calls into question whether these ERP components and their associated measures (e.g., ratio scores) can be valid indices of early auditory processing impairments in schizophrenia or whether they may also reflect other processes. For example, P50 and N100 measurements are sensitive to a variety of psychological states, including natural fluctuations in attention and vigilance over the course of a lab session (White & Yee, 2006), top-down modulation of voluntary attention (Yee et al., 2010), and acute stress (White & Yee, 1997; Yee & White, 2001).

Whether or not an individual has current, recent, or distal past experiences of auditory hallucinations may represent a further influence on P50 and N100. Psychosis and the experience of psychotic symptoms, including hallucinations, can be considered a particularly heightened

state of assigning aberrant salience (Kapur, 2003). Periods of acute psychosis often fluctuate episodically over the course of schizophrenia, with corresponding fluctuations in the extent to which aberrant salience interferes with other processes. As described above, aberrant auditory salience processing may represent a mechanism that contributes to both auditory hallucinatory experiences and early auditory processing impairments manifested in P50 and N100 ERP components. A recent experience of auditory hallucinations may indicate a period of vulnerability for heightened aberrations in salience processing, which could influence auditory ERP responses. A consequence of such an influence is that, in the context of an intervention study (e.g., Study 1), ERP measurements at follow-up may reflect more than whether CT was capable of inducing stable changes to the ERP components and their associated sensory-perceptual processes, and instead may reflect fluctuations in clinical symptoms that are independent of response to CT.

Study Overview & Hypotheses

Determining whether an intervention, such as CT, will foster changes in ERP markers of auditory processing impairments requires ruling out that any changes are not better attributed to non-intervention factors. Despite research supporting the stability of compromised P50 gating and N100 amplitude as candidate biomarkers or endophenotypes of early auditory processing impairments in schizophrenia and their potential utility for tracking intervention-related changes (Dondé et al., 2023; Freedman et al., 2003; Miller & Rockstroh, 2013, 2016; Turetsky et al., 2007, 2008), the measures have been shown to be susceptible to state influences (White & Yee, 1997, 2006; Yee et al., 2010). Thus, there may be psychological states – the features of which overlap with fundamental cognitive and psychological processes associated with P50 and N100 – that would be particularly relevant to examine in the context of ERP stability. Aberrant auditory

salience is one such possibility, as it may contribute to the impaired generation and suppression of P50 and/or N100, typically via the detection and selection of salient auditory information for further processing and the minimization of processing of redundant, non-salient information. Aberrant auditory salience may also contribute to the experience of auditory hallucinations, occurring via the misattribution of salience toward internal thought streams. This potentially shared mechanism may indicate that, when one is currently or has recently experienced hallucinations, they are in a state of heightened aberrant salience that may influence auditory processing as reflected in P50 and N100 amplitudes. Understanding these relationships, particularly as they manifest in the early course of the illness, can be critical for monitoring intervention responses and adapting treatments as needed.

The primary goal of Study 2 was to determine the extent to which ERP measurements of auditory processing impairments in first-episode schizophrenia covary with fluctuations in auditory hallucinations, which are proposed to overlap with early auditory processing via the shared mechanism of aberrant auditory salience processing. Drawing from the sample of patients with schizophrenia who were included in Study 1, the present study incorporated additional clinical symptom ratings that were obtained prior to and three months after the start of the CT intervention study.

Based on the proposal of a shared mechanism of aberrant auditory salience, it was hypothesized that individuals with recent experiences of auditory hallucinations would have smaller P50 and N100 amplitudes to S1 and larger P50 gating ratio scores than those without similar experiences. A comparable pattern of relationships was predicted to extend to patients who had past experiences of auditory hallucinations, signaling a vulnerability factor for auditory impairments. These relationships were expected to remain significant after controlling for

hallucinations in other sensory domains, other positive symptoms, and general cognitive functioning, providing evidence of a unique relationship between hallucinations and early sensory processing in the auditory modality.

It was further hypothesized that auditory salience processing would moderate the association between auditory and cognitive change following CT, such that, independent of any cognitive changes, individuals who showed less improvement from baseline levels in auditory hallucinations at three- and six-month follow-ups would exhibit less improvement in auditory ERP components following six months of CT (i.e., less enhancement of P50 and N100 to S1, less reduction of P50 gating ratio).

Method

Participants

A subset of 73 participants with schizophrenia from the Study 1 sample were selected for inclusion on the basis of having sufficient available clinical data. Usable EEG and clinical data at follow-up were available for 23 of the participants, who were then included in longitudinal analyses. As in Study 1, participants with missing or unusable data for a certain predictor or outcome were deleted pairwise to maximize statistical power across analyses.

Study Design

The same general design was used as in Study 1 with a few modifications. During a clinical stabilization period of approximately three months, UCLA Aftercare staff conducted regular monitoring and clinical assessments of all patients. Upon enrollment in the intervention research study, participants underwent an extensive battery of baseline assessments of clinical symptoms, cognitive performance, and EEG measures prior to starting the CT intervention.

Clinical assessments of symptoms were repeated at a 3-month follow-up visit, and repeated with the addition of EEG and cognitive performance at a 6-month follow-up visit.

Cognitive and Clinical Assessment

Cognitive functioning was assessed using the MCCB (Nuechterlein et al., 2008) as described in Study 1. All tests, including those described below, were administered under standardized conditions by trained personnel.

Clinical symptoms were assessed during clinical stabilization and throughout treatment with the Brief Psychiatric Rating Scale (BPRS), Expanded Version (Lukoff et al., 1986; Ventura et al., 1993) The BPRS is a clinician-rated scale that was originally developed as a measure of treatment-related symptom changes among inpatients at a psychiatric hospital (Overall & Gorham, 1962). It was later expanded to better capture symptoms and functioning among outpatients with a serious mental illness (Guy, 1976; Lukoff et al., 1986; Ventura et al., 1993). Each item is rated on a scale from 1 (not present) to 7 (extremely severe) with specific instructions and anchors for each item to improve inter-rater reliability. BPRS hallucinations symptom ratings collected during the clinical stabilization period were used in present analyses to capture a patient's history of hallucinations prior to baseline testing.

Clinical symptoms were further assessed using the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984). The SAPS is a clinician-rated scale of positive symptom severity with 34 items across 4 subscales: hallucinations, delusions, bizarre behavior, and positive formal thought disorder. Each item is rated on a scale from 0 (not at all) to 5 (severe), with evidence of good interrater reliability (Moscarelli et al., 1987). For primary analyses involving auditory hallucination severity, three SAPS hallucinations subscale items specific to the auditory domain (auditory hallucinations, voices commenting, and voices conversing) were

pooled to yield a single auditory hallucination score (range = 0-15). This approach has been taken by others in the field (Gaser, 2004; Plaze et al., 2006) and is consistent with factor analytic studies demonstrating shared factor loading of these items (Peralta & Cuesta, 1999). A pooled measure of three SAPS hallucinations subscale items corresponding to other sensory domains (somatic or tactile hallucinations, olfactory hallucinations, and visual hallucinations, which also show shared factor loading; Peralta & Cuesta, 1999) was used to test the specificity of hypothesized relationships to the auditory domain. The delusions subscale was used to test the specificity of the hypothesized relationships to hallucinations versus positive symptoms more broadly.

For the goals of the present study, a limitation of the BPRS relative to the SAPS is that the BPRS hallucinations ratings do not differentiate sensory domains. As a workaround, BPRS hallucinations ratings during the clinical stabilization period were cross-referenced with baseline SAPS hallucinations items to estimate whether BPRS ratings likely reflected auditory versus non-auditory hallucinations. In the Study 2 sample, only two patients had exclusively non-auditory hallucinations on the SAPS at baseline; to maintain homogeneity in the sample, they were omitted from analyses involving past auditory hallucinations. For all others, presence of auditory hallucinations at baseline (per SAPS) suggested that BPRS hallucination ratings during the clinical stabilization period likely reflected (or at a minimum, included) auditory hallucinations and were interpreted as such.

Cognitive Training Intervention

As detailed in Study 1, participants participated in 6 months of computerized CT using the PositScience BrainHQ and SocialVille online platforms.

EEG Data Acquisition, Processing, and Analysis

EEG data were collected during the paired stimulus procedure and analyzed using the same procedures and parameters described in Study 1 to produce waveforms for scoring of P50 and N100 ERP components.

Statistical Analyses

Data were analyzed using RStudio and Blimp Studio. For each patient, SAPS auditory hallucination ratings at baseline were used as a "recent hallucination severity" score and BPRS hallucination ratings during the clinical stabilization period were averaged to yield a "past hallucination severity" score. Relationships between baseline ERP amplitudes or P50 ratio scores and auditory hallucinations were examined continuously, using Pearson correlations based on recent/past hallucination severity ratings; as well as categorically using t-tests, with participants dummy-coded into two groups based on presence vs. absence of recent/past hallucinations.

Bivariate analyses were followed by hierarchical regression models to probe the specificity of the hypothesized relationships to the auditory domain. This strategy provided analysis of separable relationships between auditory ERP components, clinical symptoms assessed with the SAPS (auditory hallucinations, non-auditory hallucinations, delusions; measured using SAPS), and cognitive performance reflected in the MCCB Composite score. Given imbalances in subgroup sizes, HC3 heteroskedasticity-robust standard errors were used (Rajh-Weber et al., 2026).

Multilevel growth modeling was used to examine individual participants' baseline-to-follow-up changes in P50 gating ratios, P50 and N100 amplitudes, MCCB Composite scores, and auditory hallucination scores and to explore potential moderating relationships of hallucinations on intervention-related auditory and cognitive changes. Repeated auditory, clinical, and cognitive measures were treated as Level 1 variables nested within individuals (Level 2). Study visit

(baseline vs. follow-ups) was converted into a continuous ratio-scale time variable (month; 0, 3, or 6) and was included as a Level 1 predictor. Level 1 variables not collected at the 3-month follow-up visit were handled under a full-information maximum likelihood framework assuming missingness due to study design. Random intercepts and slopes for time were specified to examine longitudinal trends of interest. Models were estimated using the same MCMC algorithm and specifications described in Study 1.

Results

Participants

BPRS data were available for 73 participants, with 63 (86%) experiencing auditory hallucinations at some point during their clinical stabilization period (average severity = 3.55 on a 1-7 scale). Baseline SAPS data were available for 56 of these 63 participants, with 38 (60% of participants with SAPS data) still experiencing auditory hallucinations at the time of their baseline EEG testing prior to the start of the CT intervention (average severity = 8.51 on a pooled 0-15 scale) and 18 (29%) had remitted. Other clinical characteristics and demographics are largely the same as for the full patient group reported in Table 1 of Study 1.

Baseline Relationships between Hallucinations and Auditory Processing

Baseline mean ERP amplitudes and ratio scores as a function of presence vs. absence of auditory hallucinations are presented in Tables 6a-b. As predicted, baseline P50 ratio scores were larger (indicative of poorer gating) among individuals with recent auditory hallucinations at baseline or past auditory hallucinations during their clinical stabilization period than for individuals with no recent or past auditory hallucinations, respectively (see Figure 3). A 2×2 Recent Hallucination × Stimulus repeated-measures ANOVA on P50 amplitudes confirmed an interaction, $F(1,58) = 4.41$, $p = .04$. Simple-effects tests revealed a smaller average S1-S2 P50

Table 6a. Baseline auditory ERP measures grouped by presence (+) or absence (-) of auditory hallucinations at baseline (AH "Recent")

	AH Recent + M (SD)	**AH Recent –** M (SD)	*t*-statistic	df	*p*-value
S1 P50, μV[a]	2.30 (1.68)	2.81 (1.25)	-1.36	54.26	.18
S2 P50, μV[a]	1.28 (1.05)	1.08 (0.78)	0.88	54.24	.39
S2/S1 P50 ratio score[a]	0.71 (0.59)	0.42 (0.37)	2.34	57.44	.02
S1 N100, μV[b]	-4.03 (2.87)	-3.85 (3.77)	-0.21	41.76	.84

[a] AH Recent+ (n = 38) and AH Recent– (n = 22)
[b] AH Recent+ (n = 38) and AH Recent– (n = 25)

Table 6b. Baseline auditory ERP measures grouped by presence (+) or absence (-) of auditory hallucinations during the clinical stabilization period (AH "Past")

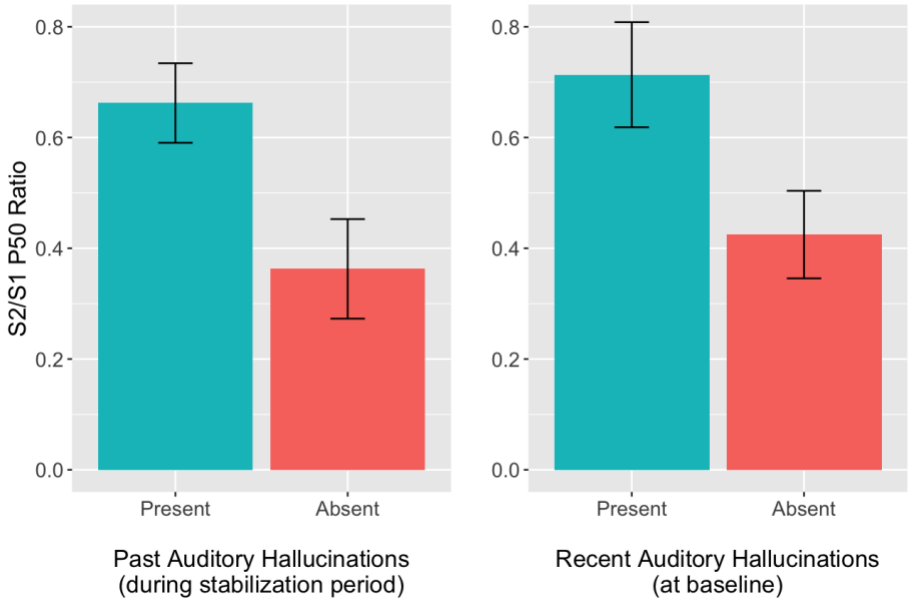
	AH Past + M (SD)	**AH Past –** M (SD)	*t*-statistic	df	*p*-value
S1 P50, μV[a]	2.44 (1.55)	2.54 (1.26)	-0.21	12.07	.84
S2 P50, μV[a]	1.30 (0.96)	0.90 (0.79)	1.37	11.94	.19
S2/S1 P50 ratio score[a]	0.66 (0.55)	0.36 (0.27)	2.60	20.34	.02
S1 N100, μV[b]	-3.71 (3.01)	-5.10 (3.82)	1.10	10.88	.30

[a] AH Past+ (n = 59) and AH Past– (n = 9)
[b] AH Past+ (n = 62) and AH Past– (n = 10)

amplitude difference score (reflecting less suppression) among patients with recent hallucinations, $t(58) = 4.85$, $p < .001$, $d = 0.66$, than among patients without, $t(58) = 6.33$, $p < .001$, $d = 1.65$.

Similar patterns were observed between subgroups of patients with past auditory hallucinations. Compared to patients whose auditory hallucinations remitted by EEG baseline, patients with persistent hallucinations tended to have larger P50 ratio scores (0.74 vs. 0.45, $t(35.55) = 1.95$, $p = .059$, $d = 0.52$). There was also an interaction between hallucinations and stimulus ($F(1,50) = 3.50$, $p = .067$). Smaller average S1-S2 P50 amplitude difference scores were observed for patients with persisting hallucinations, $t(50) = 4.46$, $p < .001$, $d = 0.63$, than for patients whose hallucinations remitted by baseline, $t(50) = 5.06$, $p < .001$, $d = 1.67$.

Figure 3. Baseline P50 ratio measures by hallucination subgroups. Left: grouped by presence or absence of auditory hallucinations during the clinical stabilization period (AH Past +/-). Right: grouped by presence or absence of auditory hallucinations at baseline (AH Recent +/-). Error bars represent ±1 standard error of the mean.



Subsequent analyses confirmed these findings as evidence of a unique association, as P50 ratio scores and difference scores did not differ depending on the presence or absence of non-auditory hallucinations or delusions. Differences as a function of auditory hallucinations were not observed for S1 P50, S2 P50, S1 N100, or the MCCB Composite score. No significant correlations emerged between recent or past auditory hallucination severity and any of the ERP measures.

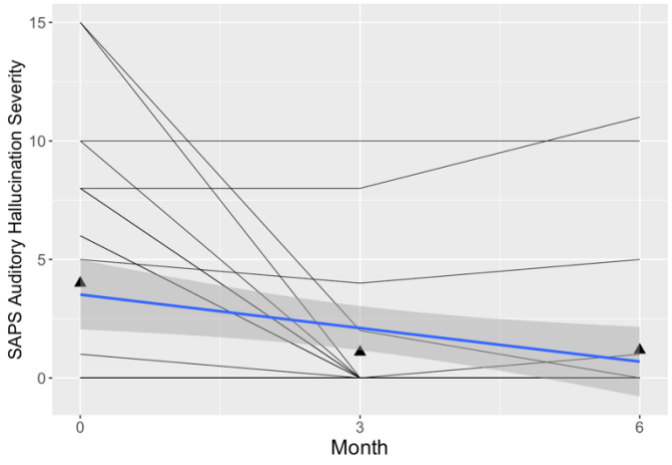
Hierarchical regression revealed that the P50 ratio score differences as a function of presence vs. absence of recent auditory hallucinations remained significant after first controlling for non-auditory hallucinations, $b = 0.32$, robust $SE = 0.15$, $t = 2.14$, $p = .037$, and after additionally controlling for baseline severity of delusions, $b = 0.36$, robust $SE = 0.18$, $t = 2.01$, $p = .049$, but fell out of the significant range once baseline general cognitive functioning was

included per a priori analytic plans, $b = 0.35$, robust $SE = 0.18$, $t = 1.96$, $p = .055$. A model including recent auditory hallucinations explained significantly more variance in baseline P50 ratio scores than a model omitting it, $\Delta R^2 = 0.078$, $F(1,55) = 4.69$, $p = .035$. Similar patterns of hierarchical regression coefficients were observed when examining presence vs. absence of past auditory hallucinations, although the model including past auditory hallucinations did not explain significantly more variance than the model omitting it, $\Delta R^2 = 0.047$, $F(1,55) = 2.70$, $p = .11$.

Longitudinal Relationships between Hallucinations and Auditory Change

Trajectories reflecting change in hallucinations are plotted in Figure 4. Multilevel growth models predicting ERP measures as a function of time (Level 1) and auditory hallucination severity (Level 1) while controlling for the effects of general cognitive functioning (Level 1) are summarized in Table 7. Models did not yield any evidence that within-person fluctuations in hallucinations were systematically associated with within-person changes in S1 P50, S1 N100, or

Figure 4. Linear model of auditory hallucination severity from baseline to 3- and 6-month follow-ups. Thin black lines represent individual patient trajectories for the full longitudinal sample; lines overlap if multiple patients showed the same pattern (e.g., a score of 0 at all three timepoints). Thick blue line represents the fitted linear trend line. Gray shaded region represents ±1 standard error around the trend line. Triangles represent mean severity at each timepoint.

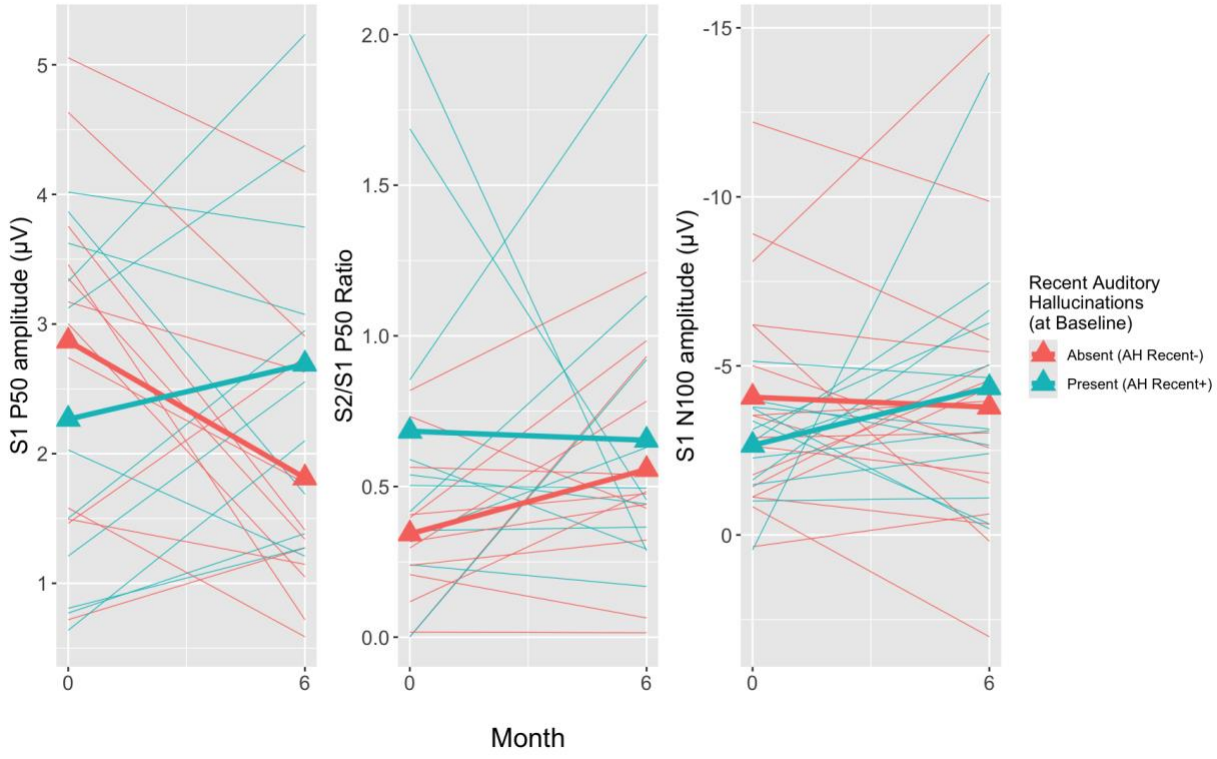


P50 ratio scores. Models were rerun on an exploratory basis replacing changes in auditory hallucination severity with baseline presence versus absence of auditory hallucinations, but relationships between auditory hallucinations and auditory changes following CT still failed to emerge (see Figure 5).

Table 7. Multilevel growth models of auditory outcomes. Month (0 or 6) included as a continuous Level 1 predictor, and auditory hallucinations and cognitive functioning each partitioned into Level 1 variability (AH-Recent$_w$ and Cognition$_w$ = within-person) around a latent Level 2 person-specific mean (AH-Recent$_b$ and Cognition$_b$ = between-person). All betas displayed are unstandardized. Boldface indicates an estimate with a credible interval that does not contain 0. CI = credible interval, Var = variance, Cov = covariance.

	Model 1: Predicting S1 P50 Amplitude		**Model 2: Predicting P50 Ratio**		**Model 3: Predicting S1 N100 Amplitude**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**2.98**	**[2.11, 3.88]**	**0.39**	**[0.07, 0.69]**	**-3.46**	**[-5.03, -1.91]**
Month	**-0.16**	**[-0.30, -0.02]**	0.06	[-0.01, 0.12]	0.01	[-0.36, 0.37]
Cognition$_w$	0.07	[-0.09, 0.23]	-0.02	[-0.08, 0.04]	0.02	[-0.33, 0.37]
Cognition$_b$	0.07	[-0.19, 0.44]	-0.01	[-0.16, 0.19]	-0.06	[-0.17, 0.06]
AH-Recent$_w$	-0.13	[-0.28, 0.02]	0.03	[-0.03, 0.09]	0.12	[-0.25, 0.48]
AH-Recent$_b$	0.27	[-1.11, 2.45]	0.00	[-0.57, 0.57]	0.09	[-0.57, 0.69]
Cognition$_w$× Month	-0.001	[-0.04, 0.04]	0.003	[-0.01, 0.02]	-0.03	[-0.15, 0.09]
AH-Recent$_w$ × Month	0.01	[-0.04, 0.06]	0.01	[-0.01, 0.03]	0.03	[-0.13, 0.19]
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	1.61	[0.33, 4.62]	0.18	[0.04, 0.53]	6.17	[1.04, 15.94]
Cov(Month,Intercept)	-0.12	[-0.47, 0.05]	-0.02	[-0.08, 0.00]	-0.28	[-1.87, 0.63]
Var(Month)	0.03	[0.00, 0.10]	0.01	[0/00, 0.02]	0.30	[0.04, 0.82]
Residual variance	0.40	[0.01, 1.36]	0.06	[0.00, 0.20]	3.79	[0.23, 10.46]
PROPORTION VARIANCE EXPLAINED						
By overall model	0.29	[0.09, 0.62]	0.33	[0.13, 0.61]	0.18	[0.06, 0.39]

Figure 5. Changes in auditory ERP outcomes from baseline to follow-up, by presence versus absence of recent hallucinations. Left: S1 P50 amplitude; Center: P50 ratio score; Right: S1 N100 amplitude (y-axis is reversed). Thin lines represent individual patient trajectories for the full longitudinal sample. Thick lines represent subgroup mean changes from baseline to follow-up. Triangles represent group means at each timepoint.



Discussion

The objective of Study 2 was to determine whether phenomenologically distinct symptoms of schizophrenia are linked by overlapping fundamental mechanisms, which could affect the efficacy of a targeted intervention such as CT. As salience processing influences early registration and filtering of sound information, it constitutes a relevant computational process in the generation and suppression of P50 and N100 ERP components (Boutros et al., 2004). At the same time, salience processing is proposed to drive auditory hallucinations via over-attribution of salience toward internal events (Kapur, 2003; Mallikarjun et al., 2018; Miyata, 2019; Palaniyappan & Liddle, 2012). By identifying a link between auditory hallucinations and early

auditory processing impairments as measured with P50 and N100, a better understanding can be achieved of factors that influence the extent to which an individual's auditory processing changes as a function of a CT intervention.

Findings from the present study support the hypothesized relationship between auditory hallucinations and auditory processing impairments, specifically with respect to sensory gating. As predicted, P50 ratio and S1-S2 amplitude difference scores were larger among patients with recent or past auditory hallucinations than among patients without auditory hallucinations. This result was not better explained by a general relationship with positive symptoms, as no differences in P50 ratio or amplitude difference scores were observed depending on whether delusions or non-auditory hallucinations were present or absent. A unique association within the auditory domain suggests that a disturbance linking these symptoms is specific to this sensory modality (Javitt & Sweet, 2015).

Early auditory processing impairments and auditory hallucinations both demonstrate associations with auditory cortex and related regions (Edgar et al., 2003; Palaniyappan et al., 2012; Popov et al., 2021; Williams et al., 2011). Therefore, auditory hallucination symptoms are likely related to breakdowns within auditory sensory-perceptual pathways. In general, sensory processing impairments are widespread in schizophrenia and affect multiple sensory domains (Adámek et al., 2022; Bansal et al., 2018b; Javitt & Freedman, 2015). The results of the present study suggest that this coupling of early sensory-perceptual processing impairments and hallucinations occurs within but not across sensory domains. Thus, non-auditory hallucinations may relate to early disruptions within corresponding non-auditory sensory domains based on shared dysfunctional mechanisms, regions, or networks.

Results from the present study cannot rule out the possibility of a competitive effect on ERP scores from active hallucinations during EEG recording. Consistent with such a possibility, symptom capture studies have shown larger P50 ratio scores during active auditory hallucinations (Thoma et al., 2017). Systematic data regarding whether any patients were actively hallucinating during the recording sessions were not available for the present study, but informal review of session tracking reports suggests that this did not occur often. Further, any incidence of concurrent hallucinations during EEG collection is more likely to affect the recent hallucinations subgroup disproportionately, but observed effects on P50 ratio extended to those with past hallucinations. To prevent potential confounding effects, future studies should aim to explicitly include and account for this information.

Dysfunction that contributes to auditory hallucinations is not limited to the auditory modality (J. Kayser et al., 2012) and may represent more general disruptions such as those that govern salience detection and attribution. Taken together, the present results are broadly reflective of a shared mechanism of aberrant hypersalience in early auditory impairments and hallucinations. This appears to largely be driven by reduced suppression of S2 among patients with recent hallucination experiences, given that differences were observed for P50 gating ratio and S1-S2 difference scores. As no significant differences were observed for S1 P50 or N100 amplitudes as a function of auditory hallucinations, it appears less likely that aberrant hyposalience broadly (Sass & Byrom, 2015) or aberrant hypersalience specifically of S1 are the linking mechanisms between these forms of auditory dysfunction in schizophrenia.

In contrast to cross-sectional associations, findings from the study's longitudinal analyses were relatively inconclusive. There was no evidence of relationships between an individual's trajectory of auditory hallucinations and CT-related changes in auditory processing impairments

for any of the assessed outcome measures. The lack of reliable covariance in pre- to post-CT changes indicates that the shared processes (e.g., aberrant auditory salience) linking gating impairments and hallucinations prior to CT may not be the mechanism of change that drives symptom improvement. This is broadly consistent with psychopharmacology research that demonstrates medication-induced reductions in positive symptoms of schizophrenia, including hallucinations, but minimal to no improvements in cognition (Lally & MacCabe, 2015). Antipsychotic medication is thought to dampen aberrant salience (Kapur, 2003), but it may do so in a more general manner that does not fully extend to early auditory processing impairments. Conversely, CT is thought to engage and strengthen aspects of low-level information pathways (Adcock et al., 2009; Popov et al., 2012; Vinogradov et al., 2012), which may improve auditory salience processing but in a more narrow manner. In either case, as symptoms or impairments in one domain improved in the present study, no systematic improvements in the other domain were observed.

It is also possible that the null longitudinal associations reflect a general lack of consistent CT-related changes in the auditory measures. Subgroup-level changes in ERPs based on recent hallucinations at baseline were modest and not reliably different from zero. Another possibility is that the null longitudinal associations reflect the relatively low base rate of auditory hallucinations persisting at the three- and six-month follow-up visits, and more broadly, the relatively low proportion of the sample for whom follow-up data were available. Hallucination severity varied widely at baseline, allowing for the detection of cross-sectional relationships with auditory ERP scores. Among those who returned, few patients remained elevated at follow-ups, which would impact the statistical power to detect any treatment-related changes that may have otherwise been observable. In contrast, individual trajectories in auditory ERP scores showed

considerable unexplained variability, which suggests that there are factors other than auditory hallucinations and cognitive functioning that influence whether an individual patient will show improvement or worsening in S1 amplitudes and gating ratio scores following CT. A larger sample with follow-up data available may have shown a clearer pattern of effects, even if the variability was just as high. However, given that observed relationships were largely not in the predicted directions and that the model-explained variance was relatively low, it is not clear that a larger sample size would have yielded significant effects.

In conclusion, although there was a clear relationship between auditory hallucinations and early auditory processing impairments pre-intervention, present findings do not support a moderating relationship between auditory hallucinations and CT-induced improvements in early auditory processing. Therefore, mechanisms inferred from baseline associations may not directly explain mechanisms of post-intervention changes, particularly if each of these variables is changing within an individual over time. Still, there is merit in exploring factors that may influence CT-related changes in biomarkers of early auditory processing impairments, particularly those with mechanistic or phenomenological overlap with impairments and/or improvements. Study 2 examined hallucinations, which fluctuated over the study period and were addressed in large part by targeted treatment with antipsychotic medications. Study 3 will examine exposure to environmental noise pollution, which was conceptualized as remaining stable over the study period and was not the focus of any interventions.

Study 3: Noise Pollution as a Potential Moderator of Intervention-Related Changes in Early Auditory Processing

One of the major tasks of the human auditory system is limiting the amount of sound from the environment that enters awareness. Without such limits, demands are placed on other regulatory systems to identify important information without over-processing information that is irrelevant. One aspect of such filtering is known as auditory sensory gating, which uses inhibitory mechanisms to screen out low-level, redundant or irrelevant inputs (Freedman et al., 1987) and is often impaired in schizophrenia (Bramon et al., 2004; Heinrichs, 2004; Patterson et al., 2008), contributing to the sensory overload that is often described by some individuals diagnosed with schizophrenia (Javitt & Freedman, 2015). Thus, auditory sensory gating helps to separate signal from noise and thereby frees up information processing resources to complete higher-order tasks required to support cognition. Failure of this system, and resultant allocation of extra cognitive resources to processing repetitive signals, decreases the capacity to process novel or relevant information more deeply and may contribute to cognitive symptoms associated with schizophrenia and other mental health conditions (Potter et al., 2005).

With respect to auditory information processing, a goal of one form of cognitive training (CT) is to reduce the auditory signal-to-noise problem by increasing the brain's processing reserves and improving the quality of the signal. When individuals are in noisy environments, however, such signal processing may be insufficient. Generally, the auditory system can readily and automatically filter out noise, but as noise levels increase, the process becomes effortful and requires selective attention (Giard et al., 2000), which can become cognitively demanding. People with impaired auditory filtering capacities, such as individuals with schizophrenia, may need to rely on effortful auditory filtering of environmental noise more often, redeploying limited cognitive resources and potentially contributing to general cognitive impairments

(Adcock et al., 2009). Thus, environmental noise may represent an important consideration with respect to auditory and cognitive processing impairment in schizophrenia. Building on the results of the previous two studies, Study 3 examined estimated levels of noise pollution at participants' residences and analyzed the extent to which this factor influenced auditory and cognitive change trajectories following CT in the Study 1 sample.

Environmental Noise and Noise Pollution

As evaluated by the United States Environmental Protection Agency (U.S. EPA; 2015), noise refers to disturbing or unwanted sound and is considered noise pollution when the noise is persistent and consequential for one's health. In general, health consequences are a function of the amount of exposure to noise, in terms of the sound level and length of time exposed. The World Health Organization (WHO; 2022) recommends an average sound pressure threshold of 70 dB over a 24-hour period, with occasional exposures of up to 100 dB for no more than 15 minutes, across all sources of noise. The recommendations encompass both controllable sources of sound (e.g., conversations, personal listening devices) and noise from personal sources (e.g., household cleaning or cooking devices), as well as persistent and often unwanted environmental noise from transportation (e.g., airplanes, jets, helicopters, trains, cars, freeways), public works (e.g., emergency sirens, construction, oil drilling, concerts), and neighborhoods (e.g., loud music, leaf blowers, power lawn mowers). Noise pollution is closely linked to urbanicity, which is an established risk factor for psychotic disorders (van Os et al., 2010), though noise is not uniform across and within cities. Uneven noise is particularly problematic for cities where planful urban design and development have not kept pace with population and noise level increases, creating pockets of noise disparity that can confer risks to residents of high-density, high-noise regions (Barrigón Morillas et al., 2018).

Health Risks Associated with Noise and Noise Pollution

Exposure to noise can have harmful effects on health depending on a variety of factors, including the sound level (whether it exceeds recommended thresholds), the time of day (especially waking versus sleeping hours), the duration of exposure, and the extent to which the exposure directly interferes with an individual's daily activities (Goines & Hagler, 2007). Hammer et al. (2014) reported that approximately 104 million individuals living in the U.S. in 2013 had continuous average sound exposure levels that exceeded WHO recommended thresholds (WHO, 2022) and were at risk for noise-induced hearing loss, which can be accompanied by tinnitus, auditory distortions, and cochlear damage as well as the cognitive impacts described above. Other adverse health effects associated with noise pollution include sleep disturbances, particularly when sleep is interrupted by continuous or intermittent noise exposure; and cardiovascular disturbances, including some evidence of heightened blood pressure and heart rate and an increased risk of cardiovascular disease, likely mediated by endocrine and autonomic responses to noise as a stressor (Goines & Hagler, 2007; Jariwala et al., 2017; van Kamp & Davies, 2013). It is worth noting that auditory processing abnormalities, sleep challenges, and cardiovascular problems are all complications commonly associated with schizophrenia, independent of any consideration of noise-related influences. Thus, the health effects associated with noise pollution may worsen known medical risks in this population.

In addition to physical health, noise pollution can have harmful effects on mental health. In a narrative review, Tortorella et al. (2022) describe a number of studies that reported relationships between increased levels of environmental noise and depression and anxiety, both when examined as categorical diagnostic outcomes or using continuous symptom severity measures. They also reported that noise exposure was associated with heightened stress, anger,

hostility, aggression, and annoyance and with lower health-related quality of life and concentration abilities. Wright et al. (2014) reviewed studies involving experimental manipulation of acute noise exposure on cognitive performance in healthy "non-clinical" adults and found broad evidence of impairments in attention, episodic memory, working memory, mental flexibility, and cognitive control in noisy conditions relative to quiet or silent conditions. As schizophrenia is associated with impairments in each of the aforementioned cognitive domains, noise exposure may result in a more pronounced negative effect on cognitive functioning in this population than is observed in the general population.

Demographic Considerations

Environmental justice researchers have proposed that the uneven distribution of environmental noise pollution disproportionately affects individuals in disadvantaged socioeconomic groups, particularly poor and racial/ethnic minority communities. For example, Nega et al. (2013) found correlations between environmental noise levels in the Minneapolis-St. Paul metropolitan region of Minnesota and household income, median household value, and the proportion of non-White residents. Casey et al. (2017) demonstrated that at the national level, census-designated regions with higher proportions of Asian, Black, and Hispanic residents have more environmental noise, a relationship that was observed across urban, suburban, and rural areas and was not better explained by poverty, education, or percent of residents who owned versus rented their homes. Similar studies have been conducted in Berlin, Germany (Lakes et al., 2013), and Montréal, Canada (L. M. Dale et al., 2015) and yielded comparable findings. The findings about noise pollution inequality add to growing bodies of work exploring the unequal distribution of environmental risk that disproportionality affects marginalized groups (for a review, see Mohai et al., 2009).

Whereas other environmental, social, and structural determinants of health have been studied in relation to schizophrenia, particularly those that disproportionately affect racial and ethnic minorities (Anglin, 2023; Anglin et al., 2021), noise pollution has received little attention. In light of inequities in the distribution of noise pollution (Casey et al., 2017; L. M. Dale et al., 2015; Lakes et al., 2013; Nega et al., 2013) and the higher incidence of psychotic disorders among ethnic, racial, and socioeconomic minorities in the U.S. (Chung et al., 2023; Lee et al., 2018; Schwartz & Blankenship, 2014), noise pollution may be an important environmental factor that can confer unique risks to individuals with schizophrenia and influence the expression and course of their illness.

Mechanisms of Noise Filtering

As noted, one of the key tasks of the auditory system is limiting the amount of sound from the physical environment that enters awareness and prioritizing relevant inputs over irrelevant ones, which is more difficult to accomplish as the amount of noise in the environment increases. In the context of background noise, the auditory system can generally adapt to the noise over time in order to gradually enhance the ability to discern and discriminate important sounds. According to computational models, this involves a number of dynamic adjustments that rely on inhibitory processing to suppress processing of noise in favor of relevant stimuli (Willmore & King, 2023), including but not limited to the sensory gating processes previously described. To support continuous noise filtering, the auditory system must process certain features of the background noise in order to maintain a representation of the noise and detect salient stimuli of interest that occur in its context, so that those stimuli can be selected and processed accordingly (C. Kayser et al., 2005). Whether or not a given sound amid the noise is deemed salient can be determined by bottom-up cues (e.g., features of the sound) or top-down

cues (e.g., auditory attention), depending on the situation (De Coensel & Botteldooren, 2010). Taken together, the ability to filter out background noise is a coordinated process that often occurs outside of awareness in order to preserve attention and cognitive resources for other task-relevant demands.

Noise filtering and auditory attention impairments in schizophrenia have been widely reported. In addition to the literature reviewed above in Study 1 regarding impaired auditory processing and sensory gating and in Study 2 regarding impaired salience attribution, most of which is based on controlled laboratory experiments conducted with simple stimuli under quiet conditions, there are a number of studies specifically examining the role of noise in the auditory and cognitive impairments seen in schizophrenia. Wright et al. (2016) found that individuals with schizophrenia showed worse performance on a cognitive battery when they completed it while listening to urban noise than when they completed the same battery in quiet conditions. Using fMRI, Tregellas et al. (2009) showed that urban white noise engages structures associated with sensory gating (e.g., superior temporal gyrus, thalamus, hippocampus, and dorsolateral prefrontal cortex), with greater activation in the latter three of these structures in participants with schizophrenia than in healthy comparison participants. They also found that activation strength correlated with EEG P50 suppression impairments, suggesting that a heightened response to noise is related to insufficient inhibitory processing. In a separate fMRI investigation involving detection of an auditory oddball tone amid urban white noise, individuals with schizophrenia showed more activation of hippocampus and less recruitment of attentional networks than comparison participants, indicative of difficulties suppressing responses to unimportant stimuli and engaging other brain regions more relevant to task demands (Tregellas et al., 2012).

In focusing on noise processing in schizophrenia, research studies have emphasized experimental manipulations of urban noise rather than adopting the broader lens of real-world noise pollution. The detection of signal from noise involves some level of maintenance of the noise representation to detect salient stimuli when they occur (C. Kayser et al., 2005). Auditory sensory gating in schizophrenia has been shown to worsen when voluntary attention is directed toward irrelevant stimuli (e.g., attending to S2; Yee et al., 2010). Noise pollution may thus be a source of auditory stimuli that is irrelevant yet ascribed heightened salience in schizophrenia. The result may be diminished or disrupted activation of the inhibitory cascade required to support sensory gating, representing a mechanism by which environmental noise may be inadequately filtered out in schizophrenia. Therefore, sensory gating capacity may be moderated by exposure to noise pollution.

Implications of Noise Filtering Impairments

The effect of noise pollution on auditory processing in schizophrenia, in turn, may contribute to cognitive symptoms. The auditory adaptation that supports efficient filtering of background noise is generally considered to occur independent of attentional focus, based largely on corresponding animal models carried out under anesthesia (Willmore & King, 2023). Similar assumptions have been made about auditory sensory gating, which has long been theorized to occur automatically and pre-attentively (Freedman et al., 1987). Although auditory sensory gating is typically impaired in schizophrenia (Bramon et al., 2004), it has been shown to improve when voluntary attention is used to support the "pre-attentive" process – even transiently normalizing gating deficits in schizophrenia (Yee et al., 2010). Thus, individuals with schizophrenia may be less able to physiologically adapt to environmental noise due to difficulties inhibiting its processing. They may therefore be more affected by noise pollution than the

general population exposed to similar noise levels, which could reduce the availability of resources to support attention to other information (including task-relevant demands) and translate to downstream cognitive difficulties.

Individuals with schizophrenia may also be more exposed to noise pollution due to inequities in its distribution across low-income and minority communities (Casey et al., 2017; L. M. Dale et al., 2015; Lakes et al., 2013; Nega et al., 2013), where they are generally more likely to reside (Chung et al., 2023; Lee et al., 2018; Schwartz & Blankenship, 2014). This has been demonstrated for other social and structural determinants of schizophrenia (Anglin, 2023; Anglin et al., 2021) but not yet examined for noise pollution despite the potentially heightened vulnerabilities described above. Risk would therefore be conferred at both the biological and environmental levels, amplifying impacts and highlighting an important public health target (Anglin et al., 2020).

The proposed relationships between environmental noise exposure and auditory and cognitive functioning in schizophrenia may also have consequential implications for intervention efficacy. Numerous factors that play a role in shaping CT response trajectories have been identified (e.g., Vita et al., 2021) and explored in Studies 1 and 2, and this information should continue to be utilized in treatment planning to the extent that it is possible. Noise pollution, and the effects it may confer on auditory processing, cognitive processing, and beyond (e.g., stress), may be yet another important consideration in determining how efficacious a treatment may be and whether any modifications or adjunctive measures are warranted. Specifically, noise exposure may impose a ceiling effect on CT interventions, limiting the amount of improvement that a patient otherwise could have made if living under other conditions. If so, this would highlight a potential gap in service delivery that may be supplemented by alternate methods,

such as mindfulness training or complementary engagement with positive soundscapes (Hahad & Beutel, 2025; Hede, 2017).

Study Overview & Hypotheses

Study 3 sought to establish a relationship between environmental noise exposure (specifically, transportation-related noise) on auditory and cognitive impairments and training-related response trajectories in first-episode schizophrenia, given the proposed framework of noise-related impacts on auditory processing and CT ceiling effects. Environmental noise exposure was estimated by cross-referencing participants' home addresses at the time of the study with data from the U.S. Department of Transportation (U.S. DOT) noise monitoring systems, relying on methods adapted from several international studies (Tortorella et al., 2022). Although this approach had limitations, including only representing a single type of noise pollution and being unable to capture historical exposure (e.g., a participant's address prior to study enrollment) or to model noise fluctuations within a given individual's period of study participation, the publicly available dataset offered a coarse approximation of noise exposure which piloting supported as a viable proxy option for the present study. Another consideration is that there are likely differences at the population level between healthy individuals and those with schizophrenia. However, exposure to high levels of noise pollution was not expected to differ by group in the present sample given the two groups were intentionally matched on primary demographic variables.

In terms of a relationship between noise pollution and auditory and cognitive functioning at baseline, it was hypothesized that, across groups, environmental noise exposure would be associated with poorer auditory processing (less P50 gating as reflected in larger ratio scores, and smaller P50 and N100 amplitudes to S1) and cognitive functioning (lower scores on MCCB and

SANS). This effect was expected to be stronger within the SZ group than the HC group, consistent with the notion that noise may exacerbate preexisting vulnerabilities.

It was further predicted that environmental noise exposure would moderate the efficacy of the intervention, such that patients in low-noise environments would experience a greater response to CT, as measured by larger improvements in cognitive functioning and auditory ERP components (greater reduction in P50 ratio scores, greater increase in P50 and N100 amplitudes to S1); whereas patients in high-noise environments would experience more modest responses to CT, as measured by smaller improvements in cognitive functioning and auditory ERP components. Such a relationship would suggest that a noisy environment can interfere with treatment progress and recovery in schizophrenia.

Method

Participants

All participants described in Study 1 were included in this study.

Study Design

The present study used the same overall design as described in Study 1.

Noise Exposure

Relying on home address data collected from all participants at both study visits, noise exposure was quantified using data from the U.S. DOT's National Transportation Noise Map (NTNM; Bureau of Transportation Statistics [BTS], 2022). The NTNM is a biennial federal initiative to map average noise trends over time related to aviation, roadway, and passenger rail. The NMTM uses simplistic modeling based on sources and input parameters, receptor specifications, and model assumptions that are tailored to each type of transportation-related noise. Data were quantified by developers using an average L_{Aeq24} metric. Values represent the

approximate noise energy (sound level, *L*, in decibels) that is recorded by receptors and weighted based on the frequencies in the normal human hearing range (*A*-weighted). It is computed as the average measurement (equivalent value, *eq*) over a stated window of time (e.g., 24 hours), with each window then averaged over the receptor's two-year data collection period to yield a single mean value for each location on the map (U.S. DOT & BTS, 2020). Noise levels below 45 dB L_{Aeq}, the lowest recommended cutoff for healthy ambient noise exposure (WHO, 2022), are not included in the DOT data set. Noise data are available as separable models for each type of noise as well as a composite, multimodal-multisource noise model that represents the mathematical sum of the acoustic data from the three noise models. The three noise models and the composite model are graphically represented using a multilayer Geographic Information System (GIS) map that can be publicly accessed at https://maps.dot.gov/BTS/NationalTransportationNoiseMap/.

Composite noise model data and documentation from 2018 and 2020 were downloaded from the BTS Geospatial Data Catalog and processed in ArcGIS Pro (version 3.2; Esri, 2023). The mosaic raster dataset was visually examined using the ArcGIS visualizer and the data inventory for California was isolated. For each participant, home address was used to set a search point within the dataset corresponding to the year closest to a participant's baseline EEG session date. Noise scores could not be obtained for 53 participants (46% of sample; 18 HC [44% of group], 35 SZ [47% of group]) due to falling below the database's noise cutoff of 45 dB L_{Aeq}, so a continuous scale could not be used for the full sample as initially planned. Instead, analyses used a dichotomous split between participants residing in "low noise" (below 45 dB L_{Aeq}) versus "high noise" (above 45 dB L_{Aeq}) environments, with follow-up analyses treating noise continuously only within the "high noise" group. Groups did not significantly differ in the proportions in the low noise versus high noise conditions, Yates-corrected $\chi^2(1) = 0.02$, $p = .88$.

Cognitive and Clinical Assessment

As described in Study 1, cognitive functioning was assessed using the MCCB (Nuechterlein et al., 2008) for all participants. Attention was also assessed for the SZ group using the Inattention subscale of the SANS (Andreasen, 1983).

Cognitive Training Intervention

The CT intervention was that described in Study 1.

EEG Data Acquisition, Processing, and Analysis

This study used the EEG data analyzed for Study 1.

Statistical Analyses

Data were analyzed using RStudio and Blimp Studio. Factorial ANOVAs with group (SZ/HC) and noise level (low/high) as between-subjects factors were used to examine differences in auditory ERP components and domains of cognitive functioning at baseline as a function of environmental noise exposure. Within the high-noise conditions, multiple regression with group (SZ/HC) as a dichotomous predictor was used to examine differential relationships between noise levels and auditory ERP components and domains of cognitive functioning at baseline.

Multilevel growth modeling was used to examine individual participants' baseline-to-follow-up changes in P50 gating ratios, P50 and N100 amplitudes, and cognitive symptom data and to explore a potential moderating role of environmental noise exposure on intervention-related auditory and cognitive changes for each group. Repeated auditory and cognitive measures were treated as Level 1 variables nested within individuals (Level 2). Study visit (baseline vs. follow-up) was converted into a continuous time variable (month, 0 or 6) and was included as a Level 1 predictor. Group (SZ vs. HC) was included as a Level 2 predictor, dummy-coded with

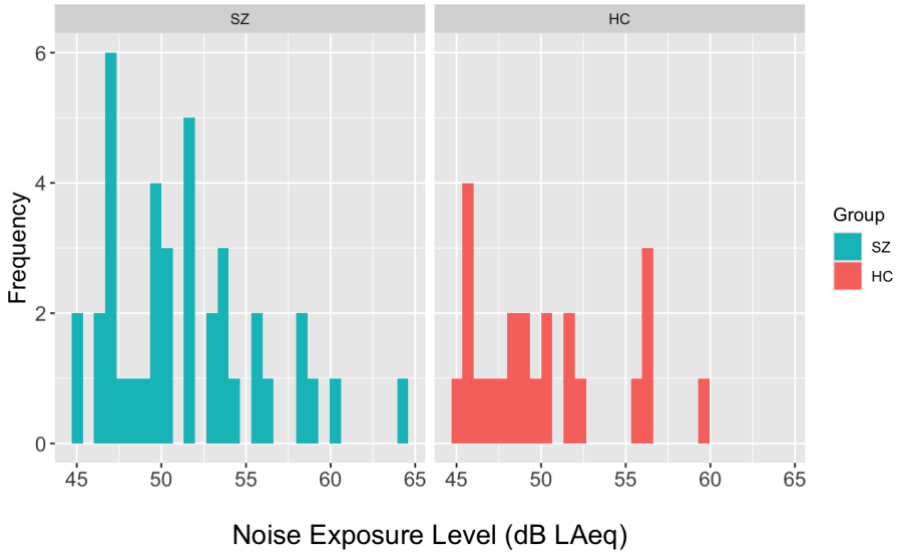
HC as the reference group. Noise (Low vs. High) was also included as a Level 2 predictor, dummy-coded with high noise as the reference group. Models were specified including a 3-way interaction term to determine whether the effect of noise on longitudinal changes differed by group. Specifically, whether any post-intervention changes (or lack thereof) observed in the SZ group were observed in the non-intervention HC group, and whether this depended on low- vs. high-noise environments. Models were estimated using the same MCMC algorithm and general specifications (burn-ins and iterations) as described in Study 1.

Results

Participants

Demographic and clinical characteristics of the sample are reported in Table 1 of Study 1. Available noise scores (i.e., within the high-noise condition) for SZ and HC are presented in Figure 6. As expected due to the demographic matching strategy, groups did not differ in mean noise exposure level, SZ = 51.5 dB L_{Aeq}, HC = 50.1 dB L_{Aeq}, $t(49.2) = 1.16$, $p = .25$.

Figure 6. Distribution of elevated noise scores within the "high noise" conditions. Left: SZ; Right: HC.



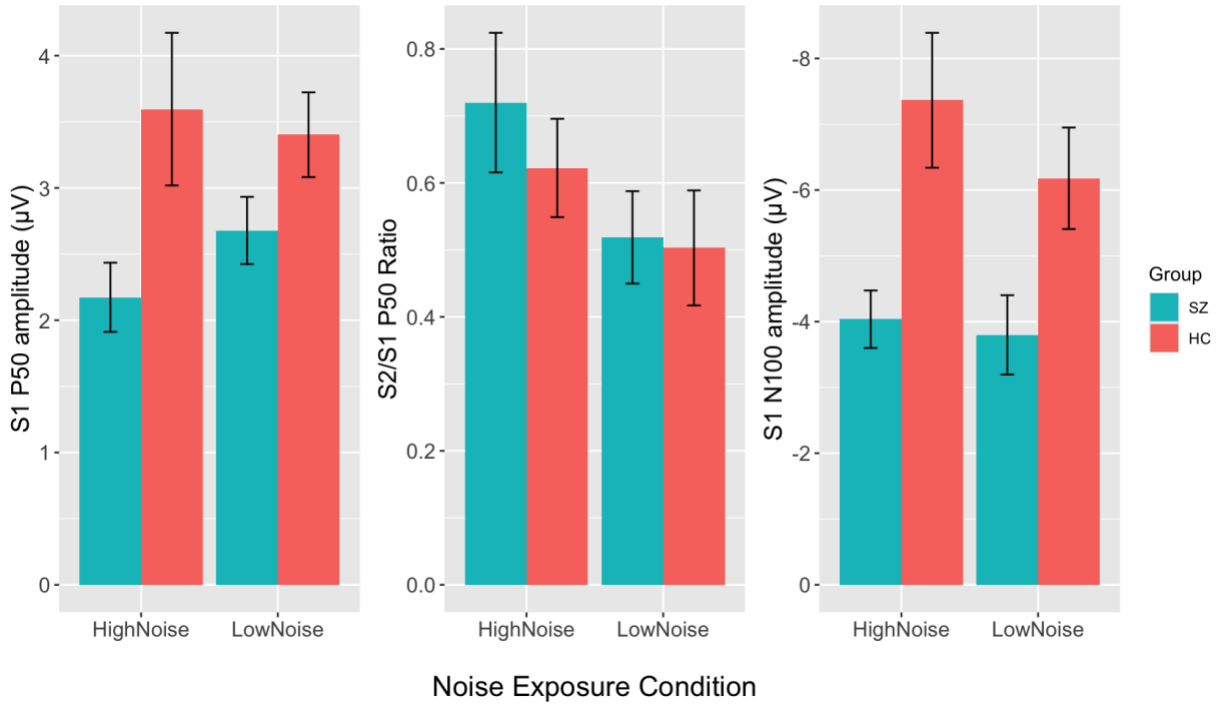
Baseline Relationships between Noise Exposure and Auditory and Cognitive Functioning

Table 8 presents baseline mean ERP amplitudes, ratio scores, and MCCB scores for each group and noise condition. Contrary to predictions, Group × Noise ANOVAs revealed no main effects of noise and no interactions for any of the ERP and cognitive measures. ERP measures are plotted in Figure 7 and depict several noteworthy findings which would be significant in a 1-tailed test, appropriate given the directional hypothesis. Across groups, a trend of larger P50 ratio scores was observed among participants residing in high-noise areas, $F(1,105) = 2.95$, $p = .089$, $\eta^2 = .03$. Although the Group x Noise interaction was not significant, $F(1,105) = 0.19$, $p = .66$, $\eta^2 = .002$, planned simple-effects tests revealed that the noise main effect for P50 ratio scores was largely driven by the SZ group, $t(105) = 1.79$, $p = .077$, $d = 0.43$, and not the HC group, $t(105) = 0.80$, $p = .42$, $d = 0.25$. For S1 P50 amplitude, simple-effects tests showed a medium-to-large

Table 8. Effects of environmental noise pollution at baseline.

	Baseline auditory/cognitive measures *M (SD)*				*(Within high-noise condition)* **Correlation with noise level**	
	SZ		**HC**			
	Low Noise *(n = 35)*	***High Noise*** *(n = 39)*	***Low Noise*** *(n = 18)*	***High Noise*** *(n = 23)*	***r***	***p***
S1 P50, μV	2.68 (1.48)	2.17 (1.55)	3.40 (1.36)	3.60 (2.71)	.04	.77
S2/S1 P50 ratio score	0.52 (0.40)	0.72 (0.62)	0.50 (0.36)	0.62 (0.34)	-.09	.50
S1 N100, μV	-3.80 (3.57)	-4.04 (2.70)	-6.18 (3.27)	-7.36 (4.92)	-.15	.26
MCCB Attention/Vigilance	39.7 (11.5)	37.3 (11.1)	44.6 (8.7)	46.7 (9.9)	-.19	.15
MCCB Processing Speed	33.6 (12.3)	34.2 (11.6)	50.1 (11.8)	52.5 (9.4)	-.11	.40
MCCB Working Memory	41.9 (12.4)	39.8 (14.4)	50.7 (9.2)	53.2 (11.1)	-.11	.42
MCCB Composite	32.0 (12.6)	32.1 (12.7)	47.3 (12.1)	50.9 (8.9)	-.14	.27
SANS Inattention	2.07 (1.16)	2.11 (1.05)	--	--	.16	.36

Figure 7. Baseline auditory ERP measures by noise condition for each group. Left: S1 P50 amplitude; Center: P50 ratio score; Right: S1 N100 amplitude (y-axis is reversed). Error bars represent ±1 standard error of the mean.



effect of group (SZ vs. HC) among participants residing in high-noise areas, $t(105) = 2.91$, $p = .004$, $d = 0.79$, and a small-to-medium but nonsignificant effect of group among participants residing in low-noise areas, $t(105) = 1.38$, $p = .17$, $d = 0.40$. For S1 N100 amplitude, both between-group (SZ vs. HC) comparisons were significant, but with a large effect among participants residing in high-noise areas, $t(110) = 3.33$, $p < .001$, $d = 0.93$, and a medium-to-large effect among participants residing in low-noise areas, $t(110) = 2.38$, $p = .02$, $d = 0.66$. Simple-effects tests of noise were not significant for either group for S1 P50 or N100 amplitudes.

Longitudinal Relationships between Noise Exposure and Auditory and Cognitive Change

Figure 8 illustrates changes in S1 P50 and N100 amplitudes and P50 ratio scores between baseline and follow-up as a function of noise condition, and Table 9 provides multilevel growth model estimates. For P50 ratio scores, there was a Noise × Month interaction, $b = 0.07$, 95% CI [0.01, 0.13], but contrary to hypotheses this was driven by participants residing in high noise areas showing more improvement in P50 ratio scores than participants residing in low noise areas. This pattern did not appear to differ between groups. Models predicting S1 P50 or N100 amplitudes did not demonstrate differences in longitudinal trajectories as a function of group, noise, or their interaction.

Figure 8. Changes in auditory ERP outcomes from baseline to follow-up, by group and noise condition. Left: S1 P50 amplitude; Center: P50 ratio score; Right: S1 N100 amplitude (y-axis is reversed). Thin lines represent individual patient trajectories for the full longitudinal sample. Thick lines represent subgroup mean changes from baseline to follow-up. Triangles represent subgroup means at each timepoint.

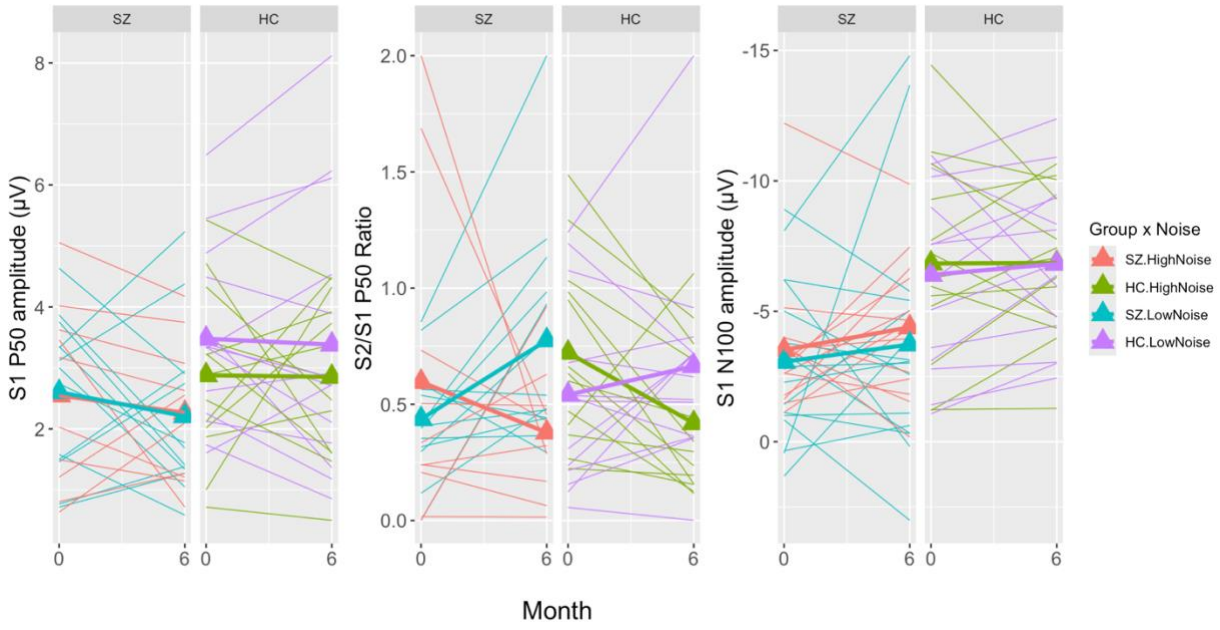


Table 9. Multilevel growth models of auditory outcomes. Group (dummy-coded HC/SZ) and Noise (dummy-coded Low/High) included as Level 2 predictors and Month (0 or 6) as a continuous Level 1 predictor. All betas displayed are unstandardized. Boldface indicates an estimate with a credible interval that does not contain 0. CI = credible interval, Var = variance, Cov = covariance.

	Model 1: Predicting S1 P50 Amplitude		**Model 2: Predicting P50 Ratio**		**Model 3: Predicting S1 N100 Amplitude**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**3.02**	**[2.30, 3.72]**	**0.72**	**[0.48, 0.94]**	**-6.85**	**[-8.49, -5.24]**
Group	-0.63	[-1.46, 0.21]	-0.11	[-0.37, 0.15]	3.36	[1.54, 5.22]
Noise	0.36	[-0.46, 1.20]	-0.17	[-0.43, 0.10]	0.46	[-1.44, 2.28]
Month	-0.01	[-0.16, 0.13]	**-0.05**	**[-0.09, -0.01]**	-0.01	[-0.33, 0.32]
Group × Month	-0.02	[-0.23, 0.18]	0.01	[-0.05, 0.08]	-0.14	[-0.58, 0.29]
Noise × Month	0.01	[-0.19, 0.20]	**0.07**	**[0.01, 0.13]**	-0.06	[-0.50, 0.37]
Group × Noise × Month	-0.05	[-0.31, 0.24]	0.03	[-0.05, 0.10]	0.09	[-0.47, 0.67]
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**1.61**	**[0.63, 2.97]**	**0.16**	**[0.05, 0.29]**	**9.07**	**[3.85, 15.94]**
Cov(Month,Intercept)	-0.06	[-0.24, 0.07]	-0.02	[-0.04, 0.00]	-0.49	[-1.42, 0.22]
Var(Month)	0.04	[0.01, 0.09]	0.004	[0.00, 0.01]	0.20	[0.02, 0.45]
Residual variance	0.55	[0.01, 1.38]	0.06	[0.00, 0.14]	2.95	[0.12, 7.36]
PROPORTION VARIANCE EXPLAINED						
By overall model	0.10	[0.02, 0.24]	0.13	[0.05, 0.23]	0.19	[0.07, 0.33]

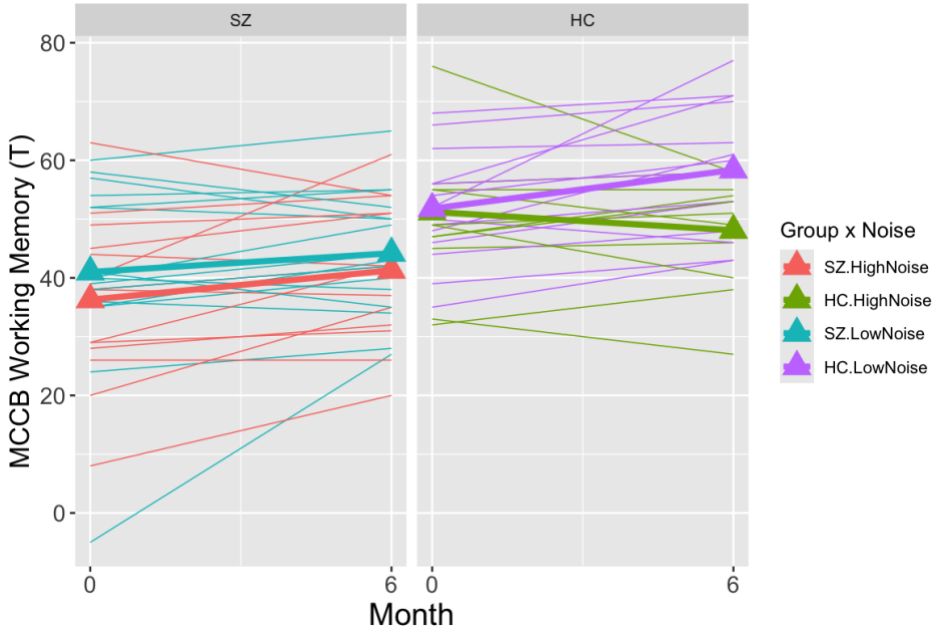
Table 10 provides model estimates for changes in cognitive outcomes between baseline and follow-up as a function of noise condition. A Group × Noise × Month interaction for working memory scores, b = 1.50, 95% CI [-2.78, -0.24], revealed that the groups differed in noise effects on working memory changes. As displayed in Figure 9, SZ in both low- and high-noise areas showed improvements in working memory following CT, with slightly larger gains among patients residing in high noise areas (slope = 0.78) than those living in low noise areas (slope = 0.59). Within the HC group, despite receiving no intervention, participants residing in low noise areas showed improvements in working memory performance over time (slope = 1.04), whereas participants in high noise areas showed a slight decline (slope = -0.27). This

Table 10. Multilevel growth models of cognitive outcomes. Group (dummy-coded HC/SZ) and Noise (dummy-coded Low/High) included as Level 2 predictors and Month (0 or 6) as a continuous Level 1 predictor. All betas displayed are unstandardized. Boldface indicates an estimate with a credible interval that does not contain 0.

	Model 1: Predicting MCCB Attention/ Vigilance		**Model 2: Predicting MCCB Processing Speed**		**Model 3: Predicting MCCB Working Memory**	
FIXED EFFECTS						
Predictor	*Beta*	*95% CI*	*Beta*	*95% CI*	*Beta*	*95% CI*
Intercept	**44.95**	**[39.8, 50.11]**	**52.21**	**[46.52, 57.95]**	**50.05**	**[43.61, 56.42]**
Group	**-8.99**	**[-14.84, -3.32]**	**-17.88**	**[-24.32, -11.52]**	**-12.79**	**[-20.03, -5.80]**
Noise	1.81	[-3.99, 7.75]	-1.60	[-8.19, 4.89]	2.92	[-4.32, 10.21]
Month	0.09	[-0.72, 0.87]	0.25	[-0.54, 1.03]	-0.27	[-1.05, 0.52]
Group × Month	0.17	[-0.88, 1.21]	0.38	[-0.64, 1.42]	**1.04**	**[0.01, 2.07]**
Noise × Month	0.16	[-0.89, 1.21]	0.87	[-0.15, 1.89]	**1.31**	**[0.27, 2.32]**
Group × Noise × Month	0.08	[-1.27, 1.44]	-1.15	[-2.37, 0.08]	**-1.5**	**[-2.78, -0.24]**
RANDOM EFFECTS						
Parameter	*Estimate*	*95% CI*	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**105.33**	**[62.73, 170.17]**	**135.79**	**[84.92, 215.83]**	**174.41**	**[112.32,273.9]**
Cov(Month,Intercept)	-3.45	[-9.73, 1.28]	**-8.10**	**[-15.90, -2.57]**	**-8.63**	**[-16.97, -2.68]**
Var(Month)	1.00	[0.08, 2.28]	**1.18**	**[0.21, 2.50]**	**1.19**	**[0.21, 2.51]**
Residual variance	15.3	[0.61, 38.39]	14.52	[0.47, 36.38]	14.94	[0.61, 37.15]
PROPORTION VARIANCE EXPLAINED						
By overall model	0.17	[0.05, 0.32]	0.44	[0.27, 0.57]	0.24	[0.10, 0.40]

	Model 4: Predicting MCCB Composite		**Model 5: Predicting SANS Inattention**	
FIXED EFFECTS				
	Beta	*95% CI*	*Beta*	*95% CI*
Intercept	**48.64**	**[42.94, 54.36]**	**1.92**	**[1.28, 2.58]**
Group	**-19.35**	**[-25.84, -12.99]**	--	--
Noise	1.28	[-5.14, 7.93]	0.48	[-0.44, 1.37]
Month	0.43	[-0.19, 1.04]	-0.09	[-0.22, 0.04]
Group × Month	0.43	[-0.38, 1.24]	--	--
Noise × Month	0.63	[-0.18, 1.43]	-0.14	[-0.31, 0.04]
Group × Noise × Month	-0.89	[-1.89, 0.12]	--	--
RANDOM EFFECTS				
	Estimate	*95% CI*	*Estimate*	*95% CI*
Var(Intercept)	**145.1**	**[95.69, 226.10]**	**0.98**	**[0.21, 2.28]**
Cov(Month,Intercept)	**-5.39**	**[-11.01, -1.35]**	-0.07	[-0.26, 0.04]
Var(Month)	**0.67**	**[0.10, 1.45]**	0.03	[0.00, 0.08]
Residual variance	**8.84**	**[0.30, 21.79]**	0.43	[0.03, 1.16]
PROPORTION VARIANCE EXPLAINED				
By overall model	0.44	[0.27, 0.58]	0.18	[0.05, 0.33]

Figure 9. Changes in MCCB Working Memory scores from baseline to follow-up, by group and noise condition. Thin lines represent individual patient trajectories for the full longitudinal sample. Thick lines represent subgroup mean changes from baseline to follow-up. Triangles represent subgroup means at each timepoint.



pattern was unique to working memory and did not emerge for the other MCCB or SANS domains. No other significant Noise × Month or Group × Noise × Month interaction effects were observed.

Discussion

To identify a potentially novel external influence on intervention response trajectories, Study 3 sought to examine relationships between an individual's auditory environment and their auditory and cognitive symptoms of schizophrenia. Many models of psychopathological functioning in schizophrenia point to the centrality of a signal-to-noise problem with regards to separating pertinent inputs and uninformative noise (Javitt & Freedman, 2015; Molina et al., 2021; Potter et al., 2005). Several studies have examined this theory using acute, distracting

noise in laboratory environments (Smucny et al., 2013; Tregellas et al., 2009, 2012; Wright et al., 2014, 2016) but to our knowledge, none has examined the effects of chronic exposure to noise in the real-world environment and how it may affect the onset or worsening of symptoms or other difficulties characteristic of the illness. The present study addressed this gap by using a publicly-available dataset to approximate noise pollution levels at participants' residences around the time of their study involvement. It was hypothesized that noise would have a deleterious effect on early auditory processing and cognition, and that noise would dampen the magnitude of patients' responses to the intervention, consistent with prior work demonstrating negative impacts of exposure to noise and noise pollution on physical and mental health (Goines & Hagler, 2007; Tortorella et al., 2022).

The results of this study offer preliminary support for a moderating role of noise exposure on auditory and cognitive processing impairments in schizophrenia. At baseline, the differences between auditory ERP measures for participants in low- versus high-noise areas primarily involved statistical trends that were fairly modest but in the expected directions and showed more notable group differences within the high-noise condition than within the low-noise condition. This pattern is consistent with the proposed model of chronic noise pollution exposure leading to disrupted capacity to initially register a novel stimulus and suppress a response to unimportant or redundant information (Tregellas et al., 2009) and can be taken as partial support for this model.

The present results additionally shed light on factors that can influence individual-level changes in auditory processing impairments. Noise exposure was a significant predictor of changes in P50 gating ratios from baseline to follow-up. Participants in high noise areas had more improvements in sensory gating over the study period than participants in low noise areas,

which was counter to the hypothesized dampening effect of noise exposure on auditory change following CT. Consistent with results of Study 1, patients who had a larger-than-average ratio score at baseline (poorer gating) tended to have a more negative slope (greater reduction in ratio score) over the course of the CT intervention. It is possible that the observed interaction effect is partially driven by a floor effect at baseline, such that individuals who are more impaired have more room for improvement. However, the interaction effect cannot be fully attributed to CT, as there were no reliable differences in mean trajectories between SZ and HC groups.

Additionally, this study provides information about the influence of noise exposure on cognition and its improvements over time and/or via intervention, particularly for working memory. Laboratory studies have demonstrated relationships between noise stimuli and transient attenuation in working memory performance (Wright et al., 2014, 2016) as well as activation in brain regions commonly associated with both sensory gating and working memory, including prefrontal cortex, hippocampus, and thalamus (Tregellas et al., 2009). Accordingly, a relationship between environmental noise and improvements in working memory impairment following CT in the present study is consistent with this literature. However, similar relationships were predicted for other cognitive domains examined in the present study, as prior work suggested there would be broad relationships between noise and attention or processing speed (Tregellas et al., 2012; Wright et al., 2016). Thus, the observed pattern of effects of noise exposure on cognition appear to be somewhat mixed relative to prior research and may require further investigation.

The pattern of differential trajectories between SZ and HC groups was also somewhat different than expected. For patients (who all received the intervention), improvements were observed regardless of noise exposure. Patients residing in low noise areas had slightly higher

working memory scores at both study visits than patients residing in high noise areas, but patients in high noise areas showed a slightly steeper slope of improvement (i.e., a slightly stronger response to the CT intervention). In contrast, a significant difference between noise conditions was observed within the HC group, in which participants residing in low noise areas showed improvements in working memory performance over time while participants residing in low noise areas showed reductions in performance. The improvement in HC participants residing in low noise areas may reflect practice effects, although these are typically small for the MCCB, even at shorter (e.g., 4-8 week) test-retest intervals (Keefe et al., 2017; Roseberry & Kristian Hill, 2014). Alternately, the reduction in working memory performance among high noise HC participants may represent the hypothesized negative effects of chronic noise exposure on cognitive functioning (Wright et al., 2014). A similar pattern might have been observed among SZ participants exposed to high noise had they not been enrolled in CT, which potentially exerted a buffering effect.

In order to more fully examine the proposed effects of noise exposure on auditory processing impairments, future research may benefit from including a more nuanced measure of exposure to noise and noise pollution. Using publicly available data from the US DOT was a cost-effective method for the present study's exploratory nature, and findings offer preliminary evidence of interesting relationships between environmental noise exposure and auditory and cognitive functioning. In terms of its limitations, the DOT's model only accounted for transportation-related noise, omitting other important sources of urban noise pollution (e.g., industrial noise; Dale et al., 2015). Additionally, the DOT model was able to sufficiently account for the influence of topography and surface conduction of sounds (U.S. Department of Transportation & Bureau of Transportation Statistics, 2020), but other critical influences on how

noise is magnified or dampened (e.g., weather, activity, and time of year) (Mennitt & Fristrup, 2016) were not considered. Thus, future investigations can expand on present findings with more comprehensive evaluations of noise pollution experienced by each participant during the duration of their study involvement.

Nevertheless, the emergence of significant differences and trending effects as a function of the present study's coarse noise approximations provides support for the viability of the overall analytic strategy and hypotheses. The detection of relationships even when using an imprecise measure of noise pollution suggests that meaningful variance exists and can be extracted in future studies. Continued efforts within this domain can support the development of more refined methods for quantifying noise exposure that address the limitations described above. In doing so, the field can begin to characterize the full scope of noise exposure's impacts on the health and functioning of the population, particularly among vulnerable or marginalized groups who may be disproportionately burdened, and guide interventions and policy initiatives to ameliorate its negative effects.

General Discussion

The three studies in the present dissertation aimed to identify moderating relationships among factors that are proposed to be mechanistically linked to auditory and cognitive impairment and treatment-related improvement in first-episode schizophrenia. Understanding factors that impact intervention response is critical to improving patient outcomes and promoting functional recovery, particularly cognitive symptoms of schizophrenia due to their strong influence on long-term functioning and quality of life (Green et al., 2004). It was hypothesized that CT would lead to improvements in markers of early auditory processing, which would facilitate improvements in higher-order cognitive functioning (Study 1) and that these relationships would be moderated by auditory hallucinations (Study 2) and exposure to noise pollution (Study 3).

Cross-Sectional Relationships

Results within and across studies provided broad support for proposed causal relationships between sensory, cognitive, clinical, and environmental domains at baseline. Notably, the SZ group had smaller P50 and N100 responses to S1 and less suppression of P50 to S2 than the HC group. Those findings are consistent with much of the literature on P50 gating and N100 in schizophrenia. As hypothesized for the SZ group, less suppression of P50 to S2 was observed among patients experiencing auditory hallucinations that persisted from the clinical stabilization phase to the baseline assessment, both when compared to patients who never experienced hallucinations and when compared to patients with a history of hallucinations that remitted by baseline. Living in a high noise pollution area was associated with a statistical trend of larger between-group differences in P50 gating and in S1 P50 and N100 amplitudes in the predicted directions.

Other patterns of differences in early auditory markers varied in ways that diverged from study hypotheses, suggesting a more nuanced and differentiated pattern of auditory abnormalities than anticipated. For example, the elements of auditory processing that differentiated the SZ and HC groups in Study 1 (primarily S1 P50 and N100 amplitudes) were not the same as those that differentiated SZ subgroups in Study 2 (primarily P50 ratio scores). This indicates that for some factors, relatively specific aspects of auditory processing are implicated. They may depend to a large extent on the constructs included in each of the comparisons, as opposed to all factors demonstrating a broader, more generalized auditory processing deficit in schizophrenia, as initially expected. Further, there were patterns of findings in the present studies that diverged from hypotheses as well as from prior literature. For example, Study 1 found significant auditory-cognitive relationships for S1 P50 and N100 amplitudes, consistent with several previous reports (Lijffijt et al., 2009; A. K. Smith et al., 2010); but no relationships for P50 ratio scores, which have been previously demonstrated across studies (Hamilton et al., 2018; A. K. Smith et al., 2010; Yee et al., 1998). The broader literature remains mixed, indicating that observed relationships may not emerge uniformly across samples or study designs. Nonetheless, pending replication, these findings extend research on auditory processing in schizophrenia and offer insights into heterogeneity in associations based on internal and external influences.

Collectively, cross-sectional findings from the present set of studies refine current models of auditory sensory gating function and dysfunction in schizophrenia across multiple levels and domains. In general, auditory inputs from the environment are detected, registered, and pre-processed by the auditory system. Inputs that are novel or salient (either inherently or due to a listener's task/goal) are attended to and processed further for use in supporting higher-order cognitive functions. Inputs that are redundant or irrelevant typically receive less attention and

processing, in part due to an automatic inhibitory cascade initiated during the processing of the initial input. This coordinated process relies on intact capacities in the registration of sound inputs, the detection and tagging of salient information, and the inhibition of processing of unremarkable information.

Within this staged and sequential model of auditory processing, present findings suggest an integrative framework in which schizophrenia is associated with less registration and processing of initial inputs and less activation of the inhibitory mechanism, contributing to heightened processing of the repeated inputs and thus less sensory gating, as has been shown in this dissertation as well as prior literature. Such variations have previously been associated with a wide range of cognitive symptoms in schizophrenia, although the strength of these relationships varies across domains. The present findings support a key role of initial input processing (versus processes involving the repeated inputs) in the associations with lower cognitive performance, generally and in the specific domains of inattention, poorer working memory, and slowed processing speed.

The proposed integrative framework also incorporates two factors that have been largely overlooked in the research literature despite their relevance when evaluating early auditory processing impairments in schizophrenia. The framework captures influences of external environment factors, which can shape the functioning of the internal auditory system. Exposure to high levels of noise pollution is associated with amplified deviations from typical expectations across each of the component processes, which suggests widespread cumulative effects of chronic noise on the integrity of auditory processing. The necessity of constant filtering of irrelevant noise inputs likely overwhelms a system that is already weakened due to illness-related dysfunction, contributing to further impairment.

The framework also captures relationships with other symptom clusters in schizophrenia. Recent and past experiences of auditory hallucinations are associated with less activation of the inhibitory mechanism and more processing of repeated inputs, but notably not with less registration and processing of novel inputs. This is suggestive of a narrower but shared mechanism of dysfunction in aberrant salience processing that contributes to hallucinations and gating impairments. Specifically, both appear to reflect the over-attribution of salience to signals (either extraneous internal signals or redundant external signals) that would typically be suppressed. In sum, this integrated framework illustrates how multiple interrelated processes contribute to typical auditory sensory gating and how these processes may be affected or exacerbated in schizophrenia.

Longitudinal Relationships

In contrast to cross-sectional associations between variables at pre-CT baseline, findings from longitudinal analyses were less consistent with hypothesized relationships between change trajectories across domains. Contrary to predictions, changes from baseline to six-month follow-up were not observed for any of the auditory ERP measures, reflecting minimal group-level changes for the SZ group following the CT intervention. Within groups, there was significant variability between participants in changes from baseline to follow-up. Many patients did show auditory improvements from CT, but much of this variability remained unexplained by the predictors examined in the present three studies. Baseline auditory processing did not reliably predict auditory or cognitive change trajectories, and the presence of auditory hallucinations or exposure to environmental noise pollution did not reliably predict auditory change trajectories (or lack thereof).

Longitudinal analyses in these studies faced several limitations that may have contributed to the null relationships observed despite significant findings across many baseline analyses. Studies were affected by unusually high rates of attrition, with 59% of SZ participants and 34% of HC participants unwilling or unable to return for follow-up testing. These rates are higher than is typical for non-pharmacological intervention studies in schizophrenia (approximately 20%; Szymczynska et al., 2017) and likely reflect disruptions caused by COVID-19-related shutdowns adding to more typical reasons for drop-out (e.g., voluntary discontinuation of the study or clinical trial). Therefore, differences in substantive findings between these studies' cross-sectional and longitudinal analyses may partially reflect differences in available sample sizes, which limited the statistical power to detect meaningful relationships. Although no significant baseline differences were observed between participants who did and did not return for follow-up, there is no way of knowing whether treatment response trajectories would or would not have differed.

The longitudinal analyses may also have been limited by an assumption of uniformity in CT participation across patients. An individual's level of engagement in treatment is often considered a key factor influencing outcomes and can be measured through simple objective proxies such as attendance or more subjective self-report measures (Dixon et al., 2016; O'Brien et al., 2009). In CT for schizophrenia, higher session attendance has been shown to relate to better neurocognitive and functional outcomes (Best et al., 2019). In the present studies, all participants in the SZ group were conceptualized as receiving the same 6-month dose of CT despite possible differences in number of sessions attended and level of engagement. There was a trade-off between the potential benefits of including CT session attendance as an additional predictor in longitudinal models and the likely harms of overparameterization by attempting to

fit models too complex for the data (Bates et al., 2015), particularly given the sample size (Maas & Hox, 2005). Future studies with larger samples should use a more fine-grained operationalization of CT participation to determine whether a dose-response relationship drives changes in cognitive and auditory functioning.

A final limitation of present longitudinal analyses is the absence of a no-CT schizophrenia comparison group. As noted, participants in the SZ group received six months of CT, and participants in the HC group received no intervention. In effect, it was assumed that any changes in the SZ group between baseline and 6-month follow-up visits were due to the CT intervention (and the moderating effects of hallucinations or noise pollution), and the HC group was expected to remain largely stable aside from minimal time-related influences. This was not generally supported across the three studies; for the most part, participants in both groups showed similar magnitudes of change in auditory and cognitive outcomes from baseline to follow-up. Such results could be interpreted as evidence of general practice effects evident in both groups rather than intervention effects in the SZ group. Prior work suggests that MCCB practice effects are typically minimal, even at shorter intervals than used in the present studies, and generally do not differ between patient and comparison samples (Keefe et al., 2017; Roseberry & Kristian Hill, 2014). However, practice effects (overall and differential between groups) cannot be definitively ruled out in the present studies. Future studies including a comparison group consisting of participants with schizophrenia who do not receive the CT intervention would be in a better position to separate intervention effects from less specific effects.

Taken together, the present studies examined the pathophysiology associated with schizophrenia by characterizing auditory processing impairments and their potential predictors

and consequences, as well as their capacity for change with a CT intervention. These studies were innovative in their proposal of mechanistically-linked associations between domains of functioning in schizophrenia through examination of early auditory attentional and perceptual processes and their relationship to cognitive and clinical symptoms and environmental influences. Although findings were mixed, they provide compelling preliminary support for an integrated model of specific auditory dysfunction in schizophrenia. The cross-sectional relationships observed highlight promising targets for future research to better understand the extent to which these variables may serve as moderators of intervention response trajectories in schizophrenia.

References

Adámek, P., Langová, V., & Horáček, J. (2022). Early-stage visual perception impairment in schizophrenia, bottom-up and back again. *Schizophrenia*, *8*(1), 27. https://doi.org/10.1038/s41537-022-00237-9

Adcock, R. A., Dale, C., Fisher, M., Aldebot, S., Genevsky, A., Simpson, G. V., Nagarajan, S., & Vinogradov, S. (2009). When Top-Down Meets Bottom-Up: Auditory Training Enhances Verbal Memory in Schizophrenia. *Schizophrenia Bulletin*, *35*(6), 1132–1141. https://doi.org/10.1093/schbul/sbp068

Adler, L. E., Pachtman, E., Franks, R. D., Pecevich, M., Waldo, M. C., & Freedman, R. (1982). Neurophysiological evidence for a defect in neuronal mechanisms involved in sensory gating in schizophrenia. *Biological Psychiatry*, *17*(6), 639–654.

Andreasen, N. C. (1983). *Scale for the Assessment of Negative Symptoms (SANS)*. University of Iowa.

Andreasen, N. C. (1984). *Scale for the Assessment of Positive Symptoms (SAPS)*. University of Iowa.

Anglin, D. M. (2023). Racism and social determinants of psychosis. *Annual Review of Clinical Psychology*, *19*(1), 277–302. https://doi.org/10.1146/annurev-clinpsy-080921-074730

Anglin, D. M., Ereshefsky, S., Klaunig, M. J., Bridgwater, M. A., Niendam, T. A., Ellman, L. M., DeVylder, J., Thayer, G., Bolden, K., Musket, C. W., Grattan, R. E., Lincoln, S. H., Schiffman, J., Lipner, E., Bachman, P., Corcoran, C. M., Mota, N. B., & van der Ven, E. (2021). From womb to neighborhood: A racial analysis of social determinants of psychosis in the United States. *American Journal of Psychiatry*, appi.ajp.2020.2. https://doi.org/10.1176/appi.ajp.2020.20071091

Anglin, D. M., Galea, S., & Bachman, P. (2020). Going Upstream to Advance Psychosis Prevention and Improve Public Health. *JAMA Psychiatry*, *77*(7), 665–666. https://doi.org/10.1001/jamapsychiatry.2020.0142

Bansal, S., Ford, J. M., & Spering, M. (2018a). The function and failure of sensory predictions. *Annals of the New York Academy of Sciences*, *1426*(1), 199–220. https://doi.org/10.1111/nyas.13686

Bansal, S., Ford, J. M., & Spering, M. (2018b). The function and failure of sensory predictions. *Annals of the New York Academy of Sciences*, *1426*(1), 199–220. https://doi.org/10.1111/nyas.13686

Barch, D. M. (2005). The cognitive neuroscience of schizophrenia. *Annual Review of Clinical Psychology*, *1*(1), 321–353. https://doi.org/10.1146/annurev.clinpsy.1.102803.143959

Barrigón Morillas, J. M., Gozalo, G. R., González, D. M., Moraga, P. A., & Vílchez-Gómez, R. (2018). Noise pollution and urban planning. *Current Pollution Reports*, *4*(3), 208–219. https://doi.org/10.1007/s40726-018-0095-7

Bates, D., Kliegl, R., Vasishth, S., & Baayen, H. (2015). Parsimonious Mixed Models. *arXiv.Org*. https://arxiv.org/abs/1506.04967v2

Best, M. W., & Bowie, C. R. (2017). A review of cognitive remediation approaches for schizophrenia: From top-down to bottom-up, brain training to psychotherapy. *Expert Review of Neurotherapeutics*, *17*(7), 713–723. https://doi.org/10.1080/14737175.2017.1331128

Best, M. W., Milanovic, M., Tran, T., Leung, P., Jackowich, R., Gauvin, S., Leibovitz, T., & Bowie, C. R. (2019). Motivation and engagement during cognitive training for

schizophrenia spectrum disorders. *Schizophrenia Research: Cognition*, *19*, 100151. https://doi.org/10.1016/j.scog.2019.100151

Boutros, N. N., Brockhaus-Dumke, A., Gjini, K., Vedeniapin, A., Elfakhani, M., Burroughs, S., & Keshavan, M. (2009). Sensory-gating deficit of the N100 mid-latency auditory evoked potential in medicated schizophrenia patients. *Schizophrenia Research*, *113*(2), 339–346. https://doi.org/10.1016/j.schres.2009.05.019

Boutros, N. N., Korzyukov, O., Jansen, B., Feingold, A., & Bell, M. (2004). Sensory gating deficits during the mid-latency phase of information processing in medicated schizophrenia patients. *Psychiatry Research*, *126*(3), 203–215. https://doi.org/10.1016/j.psychres.2004.01.007

Bowers, B., & Freedman, D. X. (1966). "Psychedelic" experiences in acute psychoses. *Archives Of General Psychiatry*, *15*, 240–248.

Bowie, C. R., Bell, M. D., Fiszdon, J. M., Johannesen, J. K., Lindenmayer, J.-P., McGurk, S. R., Medalia, A. A., Penadés, R., Saperstein, A. M., Twamley, E. W., Ueland, T., & Wykes, T. (2020). Cognitive remediation for schizophrenia: An expert working group white paper on core techniques. *Schizophrenia Research*, *215*, 49–53. https://doi.org/10.1016/j.schres.2019.10.047

Bowie, C. R., & Harvey, P. (2005). Cognition in schizophrenia: Impairments, determinants, and functional importance. *The Psychiatric Clinics of North America*, *28*, 613–633, 626. https://doi.org/10.1016/j.psc.2005.05.004

Bramon, E., Rabe-Hesketh, S., Sham, P., Murray, R. M., & Frangou, S. (2004). Meta-analysis of the P300 and P50 waveforms in schizophrenia. *Schizophrenia Research*, *70*(2–3), 315–329. https://doi.org/10.1016/j.schres.2004.01.004

Brekke, J., Kay, D. D., Lee, K. S., & Green, M. F. (2005). Biosocial pathways to functional outcome in schizophrenia. *Schizophrenia Research*, *80*(2–3), 213–225. https://doi.org/10.1016/j.schres.2005.07.008

Brenner, C. A., Kieffaber, P. D., Clementz, B. A., Johannesen, J. K., Shekhar, A., O'Donnell, B. F., & Hetrick, W. P. (2009). Event-related potential abnormalities in schizophrenia: A failure to "gate in" salient information? *Schizophrenia Research*, *113*(2), 332–338. https://doi.org/10.1016/j.schres.2009.06.012

Buchanan, Robert. W., & Carpenter, W. T. (1994). Domains of psychopathology: An approach to the reduction of heterogeneity in schizophrenia. *The Journal of Nervous and Mental Disease*, *182*(4), 193–204.

Casey, J. A., Morello-Frosch, R., Mennitt, D. J., Fristrup, K., Ogburn, E. L., & James, P. (2017). Race/ethnicity, socioeconomic status, residential segregation, and spatial variation in noise exposure in the contiguous United States. *Environmental Health Perspectives*, *125*(7), 077017. https://doi.org/10.1289/EHP898

Chang, W.-P., Arfken, C. L., Sangal, M. P., & Boutros, N. N. (2011). Probing the relative contribution of the first and second responses to sensory gating indices: A meta-analysis. *Psychophysiology*, *48*(7), 980–992. https://doi.org/10.1111/j.1469-8986.2010.01168.x

Chang, X., Zhao, W., Kang, J., Xiang, S., Xie, C., Corona-Hernández, H., Palaniyappan, L., & Feng, J. (2022). Language abnormalities in schizophrenia: Binding core symptoms through contemporary empirical evidence. *Schizophrenia*, *8*(1), 95. https://doi.org/10.1038/s41537-022-00308-x

Chung, W., Jiang, S.-F., Milham, M. P., Merikangas, K. R., & Paksarian, D. (2023). Inequalities in the incidence of psychotic disorders among racial and ethnic groups. *American Journal of Psychiatry*, appi.ajp.20220917. https://doi.org/10.1176/appi.ajp.20220917

Correll, C. U., & Schooler, N. R. (2020). Negative symptoms in schizophrenia: A review and clinical guide for recognition, assessment, and treatment. *Neuropsychiatric Disease and Treatment*, *Volume 16*, 519–534. https://doi.org/10.2147/NDT.S225643

Dale, C. L., Brown, E. G., Fisher, M., Herman, A. B., Dowling, A. F., Hinkley, L. B., Subramaniam, K., Nagarajan, S. S., & Vinogradov, S. (2015). Auditory cortical plasticity drives training-induced cognitive changes in schizophrenia. *Schizophrenia Bulletin*, sbv087. https://doi.org/10.1093/schbul/sbv087

Dale, L. M., Goudreau, S., Perron, S., Ragettli, M. S., Hatzopoulou, M., & Smargiassi, A. (2015). Socioeconomic status and environmental noise exposure in Montreal, Canada. *BMC Public Health*, *15*(1), 205. https://doi.org/10.1186/s12889-015-1571-2

De Coensel, B., & Botteldooren, D. (2010). A model of saliency-based auditory attention to environmental sound. *Proceedings of International Congress on Acoustics*, *20*, 1–8.

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*(1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009

Dixon, L. B., Holoshitz, Y., & Nossel, I. (2016). Treatment engagement of individuals experiencing mental illness: Review and update. *World Psychiatry*, *15*(1), 13–20. https://doi.org/10.1002/wps.20306

Dondé, C., Kantrowitz, J. T., Medalia, A., Saperstein, A. M., Balla, A., Sehatpour, P., Martinez, A., O'Connell, M. N., & Javitt, D. C. (2023). Early auditory processing dysfunction in

schizophrenia: Mechanisms and implications. *Neuroscience & Biobehavioral Reviews*, *148*, 105098. https://doi.org/10.1016/j.neubiorev.2023.105098

Edgar, J. C., Huang, M. X., Weisend, M. P., Sherwood, A., Miller, G. A., Adler, L. E., & Cañive, J. M. (2003). Interpreting abnormality: An EEG and MEG study of P50 and the auditory paired-stimulus paradigm. *Biological Psychology*, *65*(1), 1–20. https://doi.org/10.1016/S0301-0511(03)00094-2

Enders, C. K., Keller, B. T., Du, H., & Levy, R. (2023). *Blimp version 3.2.2* [Computer software]. https://www.appliedmissingdata.com/blimp

Esri. (2023). *ArcGIS Pro version 3.2* [Computer software]. Esri. https://www.esri.com/en-us/arcgis/products/arcgis-pro/overview

First, M., Williams, J. B. W., Karg, R. S., & Spitzer, R. L. (2015). *Structured clinical interview for DSM-5 – Research version (SCID-5-RV)*. American Psychiatric Association.

Fisher, M., Herman, A., Stephens, D. B., & Vinogradov, S. (2016). Neuroscience-informed computer-assisted cognitive training in schizophrenia: Cognitive training in schizophrenia. *Annals of the New York Academy of Sciences*, *1366*(1), 90–114. https://doi.org/10.1111/nyas.13042

Fisher, M., Holland, C., Merzenich, M. M., & Vinogradov, S. (2009). Using neuroplasticity-based auditory training to improve verbal memory in schizophrenia. *American Journal of Psychiatry*, *166*(7), 805–811. https://doi.org/10.1176/appi.ajp.2009.08050757

Fivel, L., Mondino, M., Brunelin, J., & Haesebaert, F. (2023). Basic auditory processing and its relationship with symptoms in patients with schizophrenia: A systematic review. *Psychiatry Research*, *323*, 115144. https://doi.org/10.1016/j.psychres.2023.115144

Force, R. B., Venables, N. C., & Sponheim, S. R. (2008). An auditory processing abnormality specific to liability for schizophrenia. *Schizophrenia Research*, *103*(1), 298–310. https://doi.org/10.1016/j.schres.2008.04.038

Ford, J. M., & Mathalon, D. H. (2004). Electrophysiological evidence of corollary discharge dysfunction in schizophrenia during talking and thinking. *Journal of Psychiatric Research*, *38*(1), 37–46. https://doi.org/10.1016/S0022-3956(03)00095-5

Ford, J. M., & Mathalon, D. H. (2005). Corollary discharge dysfunction in schizophrenia: Can it explain auditory hallucinations? *International Journal of Psychophysiology*, *58*(2–3), 179–189. https://doi.org/10.1016/j.ijpsycho.2005.01.014

Freedman, R., Adler, L. E., Gerhardt, G. A., Waldo, M., Baker, N., Rose, G. M., Drebing, C., Nagamoto, H., Bickford-Wimer, P., & Franks, R. (1987). Neurobiological studies of sensory gating in schizophrenia. *Schizophrenia Bulletin*, *13*(4), 669–678. https://doi.org/10.1093/schbul/13.4.669

Freedman, R., Olincy, A., Ross, R. G., Waldo, M. C., Stevens, K. E., Adler, L. E., & Leonard, S. (2003). The genetics of sensory gating deficits in schizophrenia. *Current Psychiatry Reports*, *5*(2), 155–161. https://doi.org/10.1007/s11920-003-0032-2

Fritz, J. B., Elhilali, M., David, S. V., & Shamma, S. A. (2007). Auditory attention—Focusing the searchlight on sound. *Current Opinion in Neurobiology, Sensory Systems*, *17*(4), 437–455. https://doi.org/10.1016/j.conb.2007.07.011

Gaser, C. (2004). Neuroanatomy of "hearing voices": A frontotemporal brain structural abnormality associated with auditory hallucinations in schizophrenia. *Cerebral Cortex*, *14*(1), 91–96. https://doi.org/10.1093/cercor/bhg107

Giard, M.-H., Fort, A., Mouchetant-Rostaing, Y., & Pernier, J. (2000). Neurophysiological mechanisms of auditory selective attention in humans. *Frontiers in Bioscience*, *5*, 84–94.

Gierhan, S. M. E. (2013). Connections for auditory language in the human brain. *Brain and Language*, *127*(2), 205–221. https://doi.org/10.1016/j.bandl.2012.11.002

Goines, L., & Hagler, L. (2007). Noise pollution: A modern plague. *Southern Medical Journal*, *100*(3), 287–294.

Gold, J. M., Robinson, B., Leonard, C. J., Hahn, B., Chen, S., McMahon, R. P., & Luck, S. J. (2018). Selective attention, working memory, and executive function as potential independent sources of cognitive dysfunction in schizophrenia. *Schizophrenia Bulletin*, *44*(6), 1227–1234. https://doi.org/10.1093/schbul/sbx155

Green, M. F., Kern, R. S., & Heaton, R. K. (2004). Longitudinal studies of cognition and functional outcome in schizophrenia: Implications for MATRICS. *Schizophrenia Research*, *72*(1), 41–51. https://doi.org/10.1016/j.schres.2004.09.009

Guterman, Y., Josiassen, R. C., & Bashore, T. R. (1992). Attentional influence on the P50 component of the auditory event-related brain potential. *International Journal of Psychophysiology*, *12*(2), 197–209. https://doi.org/10.1016/0167-8760(92)90011-Y

Guy, W. (1976). *ECDEU assessment manual for psychopharmacology*. U.S. Deoartment of Health, Education, and Welfare.

Habtewold, T. D., Rodijk, L. H., Liemburg, E. J., Sidorenkov, G., Boezen, H. M., Bruggeman, R., & Alizadeh, B. Z. (2020). A systematic review and narrative synthesis of data-driven studies in schizophrenia symptoms and cognitive deficits. *Translational Psychiatry*, *10*(1), 244. https://doi.org/10.1038/s41398-020-00919-x

Hahad, O., & Beutel, M. E. (2025). Environmental noise and mental health: Could psychotherapy play a supportive role? *Journal of Psychosomatic Research*, *199*, 112446. https://doi.org/10.1016/j.jpsychores.2025.112446

Hamilton, H. K., Williams, T. J., Ventura, J., Jasperse, L. J., Owens, E. M., Miller, G. A., Subotnik, K. L., Nuechterlein, K. H., & Yee, C. M. (2018). Clinical and cognitive significance of auditory sensory processing deficits in schizophrenia. *American Journal of Psychiatry*, *175*(3), 275–283. https://doi.org/10.1176/appi.ajp.2017.16111203

Hammer, M. S., Swinburn, T. K., & Neitzel, R. L. (2014). Environmental noise pollution in the United States: Developing an effective public health response. *Environmental Health Perspectives*, *122*(2), 115–119. https://doi.org/10.1289/ehp.1307272

Hede, A. (2017). Using mindfulness to reduce the health effects of community reaction to aircraft noise. *Noise and Health*, *19*(89), 165. https://doi.org/10.4103/nah.NAH_106_16

Heinrichs, R. W. (2004). Meta-analysis and the science of schizophrenia: Variant evidence or evidence of variants? *Neuroscience & Biobehavioral Reviews*, *28*(4), 379–394. https://doi.org/10.1016/j.neubiorev.2004.06.003

Hillyard, S. A., Hink, R. F., Schwent, V. L., & Picton, T. W. (1973). Electrical signs of selective attention in the human brain. *Science*, *182*(4108), 177–180.

Irvine, D. R. F. (2018). Plasticity in the auditory system. *Hearing Research*, *362*, 61–73. https://doi.org/10.1016/j.heares.2017.10.011

Jariwala, H. J., Syed, H. S., Pandya, M. J., & Gajera, Y. M. (2017, March). Noise pollution & human health: A review. *Noise and Air Pollution: Challenges and Opportunities*.

Javitt, D. C. (2009a). Sensory processing in schizophrenia: Neither simple nor intact. *Schizophrenia Bulletin*, *35*(6), 1059–1064. https://doi.org/10.1093/schbul/sbp110

Javitt, D. C. (2009b). When doors of perception close: Bottom-up models of disrupted cognition in schizophrenia. *Annual Review of Clinical Psychology*, *5*(1), 249–275. https://doi.org/10.1146/annurev.clinpsy.032408.153502

Javitt, D. C., & Freedman, R. (2015). Sensory processing dysfunction in the personal experience and neuronal machinery of schizophrenia. *American Journal of Psychiatry*, *172*(1), 17–31. https://doi.org/10.1176/appi.ajp.2014.13121691

Javitt, D. C., & Sweet, R. A. (2015). Auditory dysfunction in schizophrenia: Integrating clinical and basic features. *Nature Reviews Neuroscience*, *16*(9), 535–550. https://doi.org/10.1038/nrn4002

Jerger, K., Biggins, C., & Fein, G. (1992). P50 suppression is not affected by attentional manipulations. *Biological Psychiatry*, *31*(4), 365–377. https://doi.org/10.1016/0006-3223(92)90230-W

Kapur, S. (2003). Psychosis as a state of aberrant salience: A framework linking biology, phenomenology, and pharmacology in schizophrenia. *American Journal of Psychiatry*, *160*(1), 13–23. https://doi.org/10.1176/appi.ajp.160.1.13

Kathmann, N., & Engel, R. R. (1990). Sensory gating in normals and schizophrenics: A failure to find strong P50 suppression in normals. *Biological Psychiatry*, *27*(11), 1216–1226. https://doi.org/10.1016/0006-3223(90)90419-3

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261–276. https://doi.org/10.1093/schbul/13.2.261

Kayser, C., Petkov, C. I., Lippert, M., & Logothetis, N. K. (2005). Mechanisms for allocating auditory attention: An auditory saliency map. *Current Biology*, *15*(21), 1943–1947. https://doi.org/10.1016/j.cub.2005.09.040

Kayser, J., Tenke, C. E., Kroppmann, C. J., Alschuler, D. M., Fekri, S., Gil, R., Jarskog, L. F., Harkavy-Friedman, J. M., & Bruder, G. E. (2012). A neurophysiological deficit in early visual processing in schizophrenia patients with auditory hallucinations. *Psychophysiology*, *49*(9), 1168–1178. https://doi.org/10.1111/j.1469-8986.2012.01404.x

Keefe, R. S. E., Davis, V. G., Harvey, P. D., Atkins, A. S., Haig, G. M., Hagino, O., Marder, S., Hilt, D. C., & Umbricht, D. (2017). Placebo Response and Practice Effects in Schizophrenia Cognition Trials. *JAMA Psychiatry*, *74*(8), 807–814. https://doi.org/10.1001/jamapsychiatry.2017.1574

Keefe, R. S. E., & Harvey, P. D. (2012). Cognitive impairment in schizophrenia. In M. A. Geyer & G. Gross (Eds.), *Handbook of Experimental Pharmacology: Novel Antischizophrenia Treatments* (Vol. 213). Springer.

Kern, R. S., Nuechterlein, K. H., Green, M. F., Baade, L. E., Fenton, W. S., Gold, J. M., Keefe, R. S. E., Mesholam-Gately, R., Mintz, J., Seidman, L. J., Stover, E., & Marder, S. R. (2008). The MATRICS Consensus Cognitive Battery, Part 2: Co-norming and standardization. *American Journal of Psychiatry*, *165*(2), 214–220. https://doi.org/10.1176/appi.ajp.2007.07010043

Knowles, E. E. M., Weiser, M., David, A. S., Glahn, D. C., Davidson, M., & Reichenberg, A. (2015). The puzzle of processing speed, memory, and executive function impairments in schizophrenia: Fitting the pieces together. *Biological Psychiatry*, *78*(11), 786–793. https://doi.org/10.1016/j.biopsych.2015.01.018

Koshiyama, D., Thomas, M. L., Miyakoshi, M., Joshi, Y. B., Molina, J. L., Tanaka-Koshiyama, K., Sprock, J., Braff, D. L., Swerdlow, N. R., & Light, G. A. (2021). Hierarchical pathways from sensory processing to cognitive, clinical, and functional impairments in schizophrenia. *Schizophrenia Bulletin*, *47*(2), 373–385. https://doi.org/10.1093/schbul/sbaa116

Lakes, T., Brückner, M., & Krämer, A. (2013). Development of an environmental justice index to determine socio-economic disparities of noise pollution and green space in residential areas in Berlin. *Journal of Environmental Planning and Management*, *57*(4), 538–556.

Lally, J., & MacCabe, J. H. (2015). Antipsychotic medication in schizophrenia: A review. *British Medical Bulletin*, *114*(1), 169–179. https://doi.org/10.1093/bmb/ldv017

Lee, C.-T., Hsiao, C., Lee, J.-F., Chen, Y., Nfor, O., Huang, J.-Y., Wang, L., Ho, C., & Liaw, Y.-P. (2018). Relationship between schizophrenia and low-income based on age and sex: Results from a nation-wide population-based longitudinal study. *Neuropsychiatry*, *08*. https://doi.org/10.4172/Neuropsychiatry.1000426

Lijffijt, M., Lane, S. D., Meier, S. L., Boutros, N. N., Burroughs, S., Steinberg, J. L., Gerard Moeller, F., & Swann, A. C. (2009). P50, N100, and P200 sensory gating: Relationships with behavioral inhibition, attention, and working memory. *Psychophysiology*, *46*(5), 1059–1068. https://doi.org/10.1111/j.1469-8986.2009.00845.x

Lopez-Calderon, J., & Luck, S. J. (2014). ERPLAB: An open-source toolbox for the analysis of event-related potentials. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00213

Lu, B. Y., Edgar, J. C., Jones, A. P., Smith, A. K., Huang, M., Miller, G. A., & Cañive, J. M. (2007). Improved test–retest reliability of 50-ms paired-click auditory gating using

magnetoencephalography source modeling. *Psychophysiology*, *44*(1), 86–90. https://doi.org/10.1111/j.1469-8986.2006.00478.x

Lu, Z., Guo, J., Sun, J., Sun, Y., Zhang, Y., Zhang, Y., Liao, Y., Kang, Z., Feng, X., Zhao, G., Yuan, R., Zhu, Y., & Yue, W. (2025). The event-related potential components across psychiatric disorders: A systematic review and network meta-analysis. *Molecular Psychiatry*, *30*(9), 4422–4431. https://doi.org/10.1038/s41380-025-03062-5

Lukoff, D., Nuechterlein, K. H., & Ventura, J. (1986). Manual for the Expanded Brief Psychiatric Rating Scale. *Schizophrenia Bulletin*, *12*, 594–602.

Maas, C. J. M., & Hox, J. J. (2005). Sufficient Sample Sizes for Multilevel Modeling. *Methodology*, *1*(3), 86–92. https://doi.org/10.1027/1614-2241.1.3.86

Mallikarjun, P. K., Lalousis, P. A., Dunne, T. F., Heinze, K., Reniers, R. L., Broome, M. R., Farmah, B., Oyebode, F., Wood, S. J., & Upthegrove, R. (2018). Aberrant salience network functional connectivity in auditory verbal hallucinations: A first episode psychosis sample. *Translational Psychiatry*, *8*(1), Article 1. https://doi.org/10.1038/s41398-018-0118-6

Marchi, F. (2020). The cognitive processing hierarchy. In F. Marchi (Ed.), *The Attentional Shaping of Perceptual Experience: An Investigation into Attention and Cognitive Penetrability* (pp. 17–32). Springer International Publishing. https://doi.org/10.1007/978-3-030-33558-8_2

Marder, S. R., & Galderisi, S. (2017). The current conceptualization of negative symptoms in schizophrenia. *World Psychiatry*, *16*(1), 14–24. https://doi.org/10.1002/wps.20385

McCarthy-Jones, S., Smailes, D., Corvin, A., Gill, M., Morris, D. W., Dinan, T. G., Murphy, K. C., Anthony O′Neill, F., Waddington, J. L., Australian Schizophrenia Research Bank,

Donohoe, G., & Dudley, R. (2017). Occurrence and co-occurrence of hallucinations by modality in schizophrenia-spectrum disorders. *Psychiatry Research*, *252*, 154–160. https://doi.org/10.1016/j.psychres.2017.01.102

Medalia, A., Saperstein, A. M., Qian, M., & Javitt, D. C. (2019). Impact of baseline early auditory processing on response to cognitive remediation for schizophrenia. *Schizophrenia Research*, *208*, 397–405. https://doi.org/10.1016/j.schres.2019.01.012

Mennitt, D. J., & Fristrup, K. M. (2016). Influential factors and spatiotemporal patterns of environmental sound levels in the contiguous United States. *Noise Control Engineering Journal*, *64*(3), 342–353. https://doi.org/10.3397/1/376384

Menon, V. (2015). Salience network. In *Brain Mapping* (pp. 597–611). Elsevier. https://doi.org/10.1016/B978-0-12-397025-1.00052-X

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure and Function*, *214*(5), 655–667. https://doi.org/10.1007/s00429-010-0262-0

Mesulam, M. (1998). From sensation to cognition. *Brain*, *121*(6), 1013–1052. https://doi.org/10.1093/brain/121.6.1013

Miller, G. A., Lutzenberger, W., & Elbert, T. (1991). The linked-reference issue in EEG and ERP recording. *Journal of Psychophysiology*, *5*, 273–276.

Miller, G. A., & Rockstroh, B. (2013). Endophenotypes in psychopathology research: Where do we stand? *Annual Review of Clinical Psychology*, *9*(1), 177–213. https://doi.org/10.1146/annurev-clinpsy-050212-185540

Miller, G. A., & Rockstroh, B. (2016). Progress and Prospects for Endophenotypes for Schizophrenia in the Time of Genomics, Epigenetics, Oscillatory Brain Dynamics, and

the Research Domain Criteria. In T. Abel & T. Nickl-Jockschat (Eds.), *The Neurobiology of Schizophrenia* (pp. 17–38). Academic Press. https://doi.org/10.1016/B978-0-12-801829-3.00010-0

Miyata, J. (2019). Toward integrated understanding of salience in psychosis. *Neurobiology of Disease, What Can Clinical Findings Tell Us about the Neurobiology of Schizophrenia? Revisited*, *131*, 104414. https://doi.org/10.1016/j.nbd.2019.03.002

Mohai, P., Pellow, D., & Roberts, J. T. (2009). Environmental justice. *Annual Review of Environment and Resources*, *34*(1), 405–430. https://doi.org/10.1146/annurev-environ-082508-094348

Molina, J. L., Joshi, Y. B., Nungaray, J. A., Thomas, M. L., Sprock, J., Clayson, P. E., Sanchez, V. A., Attarha, M., Biagianti, B., Swerdlow, N. R., & Light, G. A. (2021). Central auditory processing deficits in schizophrenia: Effects of auditory-based cognitive training. *Schizophrenia Research*, *236*, 135–141. https://doi.org/10.1016/j.schres.2021.07.033

Morris, R., Griffiths, O., Le Pelley, M. E., & Weickert, T. W. (2013). Attention to irrelevant cues is related to positive symptoms in schizophrenia. *Schizophrenia Bulletin*, *39*(3), 575–582. https://doi.org/10.1093/schbul/sbr192

Moscarelli, M., Maffei, C., Cesana, B. M., Boato, P., Farma, T., Grilli, A., Lingiardi, V., & Cazzullo, C. L. (1987). An international perspective on assessment of negative and positive symptoms in schizophrenia. *The American Journal of Psychiatry*, *144*(12), 1595–1598. https://doi.org/10.1176/ajp.144.12.1595

Nagamoto, H. T., Adler, L. E., Waldo, M. C., Griffith, J., & Freedman, R. (1991). Gating of auditory response in schizophrenics and normal controls. *Schizophrenia Research*, *4*(1), 31–40. https://doi.org/10.1016/0920-9964(91)90007-E

Nega, T. H., Chihara, L., Smith, K., & Jayaraman, M. (2013). Traffic noise and inequality in the Twin Cities, Minnesota. *Human and Ecological Risk Assessment: An International Journal*, *19*(3), 601–619. https://doi.org/10.1080/10807039.2012.691409

Niznikiewicz, M. A., O'Donnell, B. F., Nestor, P. G., Smith, L., Law, S., Karapelou, M., Shenton, M. E., & McCarley, R. W. (1997). ERP assessment of visual and auditory language processing in schizophrenia. *Journal of Abnormal Psychology*, *106*(1), 85–94.

Nuechterlein, K. H., Barch, D. M., Gold, J. M., Goldberg, T. E., Green, M. F., & Heaton, R. K. (2004). Identification of separable cognitive factors in schizophrenia. *Schizophrenia Research*, *72*(1), 29–39. https://doi.org/10.1016/j.schres.2004.09.007

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D., Essock, S., Fenton, W. S., Frese, F. J., Gold, J. M., Goldberg, T., Heaton, R. K., Keefe, R. S. E., Kraemer, H., Mesholam-Gately, R., Seidman, L. J., Stover, E., Weinberger, D. R., Young, A. S., … Marder, S. R. (2008). The MATRICS Consensus Cognitive Battery, Part 1: Test selection, reliability, and validity. *American Journal of Psychiatry*, *165*(2), 203–213. https://doi.org/10.1176/appi.ajp.2007.07010042

Nuechterlein, K. H., Ventura, J., Subotnik, K. L., Hayata, J. N., Medalia, A., & Bell, M. D. (2014). Developing a cognitive training strategy for first-episode schizophrenia: Integrating bottom-up and top-down approaches. *American Journal of Psychiatric Rehabilitation*, *17*(3), 225–253. https://doi.org/10.1080/15487768.2014.935674

O'Brien, A., Fahmy, R., & Singh, S. P. (2009). Disengagement from mental health services. *Social Psychiatry and Psychiatric Epidemiology*, *44*(7), 558–568. https://doi.org/10.1007/s00127-008-0476-0

Overall, J. E., & Gorham, D. R. (1962). The Brief Psychiatric Rating Scale. *Psychological Reports*, *10*, 799–812. https://doi.org/10.2466/pr0.1962.10.3.799

Palaniyappan, L., Balain, V., Radua, J., & Liddle, P. F. (2012). Structural correlates of auditory hallucinations in schizophrenia: A meta-analysis. *Schizophrenia Research*, *137*(1), 169–173. https://doi.org/10.1016/j.schres.2012.01.038

Palaniyappan, L., & Liddle, P. F. (2012). Does the salience network play a cardinal role in psychosis? An emerging hypothesis of insular dysfunction. *Journal of Psychiatry and Neuroscience*, *37*(1), 17–27. https://doi.org/10.1503/jpn.100176

Parr, T., & Friston, K. J. (2019). Attention or salience? *Current Opinion in Psychology*, *29*, 1–5. https://doi.org/10.1016/j.copsyc.2018.10.006

Patterson, J. V., Hetrick, W. P., Boutros, N. N., Jin, Y., Sandman, C., Stern, H., Potkin, S., & Bunney, W. E. (2008). P50 sensory gating ratios in schizophrenics and controls: A review and data analysis. *Psychiatry Research*, *158*(2), 226–247. https://doi.org/10.1016/j.psychres.2007.02.009

Peralta, V., & Cuesta, M. J. (1999). Dimensional structure of psychotic symptoms: An item-level analysis of SAPS and SANS symptoms in psychotic disorders. *Schizophrenia Research*, *38*(1), 13–26.

Picton, T. W., Hillyard, S. A., Galambos, R., & Schiff, M. (1971). Human auditory attention: A central or peripheral process? *Science*, *173*(3994), 351–353. https://doi.org/10.1126/science.173.3994.351

Plaze, M., Bartrés-Faz, D., Martinot, J.-L., Januel, D., Bellivier, F., De Beaurepaire, R., Chanraud, S., Andoh, J., Lefaucheur, J.-P., Artiges, E., Pallier, C., & Paillère-Martinot, M.-L. (2006). Left superior temporal gyrus activation during sentence perception negatively correlates with auditory hallucination severity in schizophrenia patients. *Schizophrenia Research*, *87*(1), 109–115. https://doi.org/10.1016/j.schres.2006.05.005

Popov, T. G., Carolus, A., Schubring, D., Popova, P., Miller, G. A., & Rockstroh, B. S. (2015). Targeted training modifies oscillatory brain activity in schizophrenia patients. *NeuroImage: Clinical*, *7*, 807–814. https://doi.org/10.1016/j.nicl.2015.03.010

Popov, T. G., Jordanov, T., Rockstroh, B., Elbert, T., Merzenich, M. M., & Miller, G. A. (2011). Specific cognitive training normalizes auditory sensory gating in schizophrenia: A randomized trial. *Biological Psychiatry*, *69*(5), 465–471. https://doi.org/10.1016/j.biopsych.2010.09.028

Popov, T. G., Rockstroh, B., & Miller, G. A. (2021). Oscillatory connectivity as a mechanism of auditory sensory gating and its disruption in schizophrenia. *Psychophysiology*. https://doi.org/10.1111/psyp.13770

Popov, T. G., Rockstroh, B., Weisz, N., Elbert, T., & Miller, G. A. (2012). Adjusting brain dynamics in schizophrenia by means of perceptual and cognitive training. *PLoS ONE*, *7*(7), e39051. https://doi.org/10.1371/journal.pone.0039051

Potter, D., Summerfelt, A., Gold, J., & Buchanan, R. W. (2005). Review of clinical correlates of P50 sensory gating abnormalities in patients with schizophrenia. *Schizophrenia Bulletin*, *32*(4), 692–700. https://doi.org/10.1093/schbul/sbj050

Pugliese, V., de Filippis, R., Aloi, M., Rotella, P., Carbone, E. A., Gaetano, R., & De Fazio, P. (2022). Aberrant salience correlates with psychotic dimensions in outpatients with

schizophrenia spectrum disorders. *Annals of General Psychiatry*, *21*, 25. https://doi.org/10.1186/s12991-022-00402-5

Rajh-Weber, H., Huber, S. E., & Arendasy, M. (2026). Using Heteroskedasticity-Consistent Standard Errors and the Bootstrap for Linear Regression Analysis Available in SPSS: A Tutorial. *Advances in Methods and Practices in Psychological Science*, *9*(1), 25152459251408046. https://doi.org/10.1177/25152459251408046

Rissling, A. J., & Light, G. A. (2010). Neurophysiological measures of sensory registration, stimulus discrimination, and selection in schizophrenia patients. In N. R. Swerdlow (Ed.), *Current Topics in Behavioral Neurosciences: Behavioral Neurobiology of Schizophrenia and its Treatment* (Vol. 4, pp. 283–309).

Rosburg, T. (2018). Auditory N100 gating in patients with schizophrenia: A systematic meta-analysis. *Clinical Neurophysiology*, *129*(10), 2099–2111. https://doi.org/10.1016/j.clinph.2018.07.012

Rosburg, T., Boutros, N. N., & Ford, J. M. (2008). Reduced auditory evoked potential component N100 in schizophrenia—A critical review. *Psychiatry Research*, *161*(3), 259–274. https://doi.org/10.1016/j.psychres.2008.03.017

Roseberry, J. E., & Kristian Hill, S. (2014). Limited practice effects and evaluation of expectation for change: MATRICS Consensus Cognitive Battery. *Schizophrenia Research*, *159*(1), 188–192. https://doi.org/10.1016/j.schres.2014.08.004

Saks, E. (2007). *The center cannot hold: My journey through madness*. Hachette Books.

Sass, L., & Byrom, G. (2015). Phenomenological and neurocognitive perspectives on delusions: A critical overview. *World Psychiatry*, *14*(2), 164–173. https://doi.org/10.1002/wps.20205

Schiwy, L. C., Forlim, C. G., Fischer, D. J., Kühn, S., Becker, M., & Gallinat, J. (2022). Aberrant functional connectivity within the salience network is related to cognitive deficits and disorganization in psychosis. *Schizophrenia Research*, *246*, 103–111. https://doi.org/10.1016/j.schres.2022.06.008

Schwartz, R. C., & Blankenship, D. M. (2014). Racial disparities in psychotic disorder diagnosis: A review of empirical literature. *World Journal of Psychiatry*, *4*(4), 133–140. https://doi.org/10.5498/wjp.v4.i4.133

Shen, C.-L., Chou, T.-L., Lai, W.-S., Hsieh, M. H., Liu, C.-C., Liu, C.-M., & Hwu, H.-G. (2020). P50, N100, and P200 auditory sensory gating deficits in schizophrenia patients. *Frontiers in Psychiatry*, *11*, 868. https://doi.org/10.3389/fpsyt.2020.00868

Shergill, S. S., Murray, R. M., & Mcguire, P. K. (1998). Auditory hallucinations: A review of psychological treatments. *Schizophrenia Research*, *32*, 137–150.

Smith, A. K., Edgar, J. C., Huang, M., Lu, B. Y., Thoma, R. J., Hanlon, F. M., McHaffie, G., Jones, A. P., Paz, R. D., Miller, G. A., & Cañive, J. M. (2010). Cognitive abilities and 50- and 100-msec paired-click processes in schizophrenia. *American Journal of Psychiatry*, *167*(10), 1264–1275. https://doi.org/10.1176/appi.ajp.2010.09071059

Smith, D. A., Boutors, N. N., & Schwarzopf, S. B. (1994). Reliability of P50 auditory event-related potential indices of sensory gating. *Psychophysiology*, *31*(5), 495–502. https://doi.org/10.1111/j.1469-8986.1994.tb01053.x

Smucny, J., Olincy, A., Eichman, L. C., Lyons, E., & Tregellas, J. R. (2013). Early sensory processing deficits predict sensitivity to distraction in schizophrenia. *Schizophrenia Research*, *147*(1), 196–200. https://doi.org/10.1016/j.schres.2013.03.025

Szymczynska, P., Walsh, S., Greenberg, L., & Priebe, S. (2017). Attrition in trials evaluating complex interventions for schizophrenia: Systematic review and meta-analysis. *Journal of Psychiatric Research*, *90*, 67–77. https://doi.org/10.1016/j.jpsychires.2017.02.009

The MathWorks Inc. (2023). *MATLAB version: 23.2.0.2428915 (R2023b)* [Computer software]. The MathWorks Inc. https://www.mathworks.com

Thoma, R. J., Hanlon, F. M., Miller, G. A., Huang, M., Weisend, M. P., Sanchez, F. P., Waldorf, V. A., Jones, A., Smith, A., Formoso, M. J., & Cañive, J. M. (2006). Neuropsychological and sensory gating deficits related to remote alcohol abuse history in schizophrenia. *Journal of the International Neuropsychological Society*, *12*(1), 34–44. https://doi.org/10.1017/S1355617706060097

Thoma, R. J., Hanlon, F. M., Moses, S. N., Edgar, J. C., Huang, M., Weisend, M. P., Irwin, J., Sherwood, A., Paulson, K., Bustillo, J., Adler, L. E., Miller, G. A., & Cañive, J. M. (2003). Lateralization of Auditory Sensory Gating and Neuropsychological Dysfunction in Schizophrenia. *American Journal of Psychiatry*, *160*(9), 1595–1605. https://doi.org/10.1176/appi.ajp.160.9.1595

Thoma, R. J., Meier, A., Houck, J., Clark, V. P., Lewine, J. D., Turner, J., Calhoun, V., & Stephen, J. (2017). Diminished auditory sensory gating during active auditory verbal hallucinations. *Schizophrenia Research*, *188*, 125–131. https://doi.org/10.1016/j.schres.2017.01.023

Tordini, F., Bregman, A. S., Cooperstock, J. R., Ankolekar, A., & Sandholm, T. (2013). Toward an improved model of auditory saliency. *Proceedings of the International Conference on Auditory Display*, *19*, 189–196.

Tortorella, A., Menculini, G., Moretti, P., Attademo, L., Balducci, P. M., Bernardini, F., Cirimbilli, F., Chieppa, A. G., Ghiandai, N., & Erfurth, A. (2022). New determinants of mental health: The role of noise pollution. A narrative review. *International Review of Psychiatry*, *34*(7–8), 783–796. https://doi.org/10.1080/09540261.2022.2095200

Tregellas, J. R., Ellis, J., Shatti, S., Du, Y. P., & Rojas, D. C. (2009). Increased hippocampal, thalamic, and prefrontal hemodynamic response to an urban noise stimulus in schizophrenia. *American Journal of Psychiatry*, *166*(3), 354–360. https://doi.org/10.1176/appi.ajp.2008.08030411

Tregellas, J. R., Smucny, J., Eichman, L., & Rojas, D. C. (2012). The effect of distracting noise on the neuronal mechanisms of attention in schizophrenia. *Schizophrenia Research*, *142*(1), 230–236. https://doi.org/10.1016/j.schres.2012.09.008

Turetsky, B. I., Calkins, M. E., Light, G. A., Olincy, A., Radant, A. D., & Swerdlow, N. R. (2007). Neurophysiological endophenotypes of schizophrenia: The viability of selected candidate measures. *Schizophrenia Bulletin*, *33*(1), 69–94. https://doi.org/10.1093/schbul/sbl060

Turetsky, B. I., Greenwood, T. A., Olincy, A., Radant, A. D., Braff, D. L., Cadenhead, K. S., Dobie, D. J., Freedman, R., Green, M. F., Gur, R. E., Gur, R. C., Light, G. A., Mintz, J., Nuechterlein, K. H., Schork, N. J., Seidman, L. J., Siever, L. J., Silverman, J. M., Stone, W. S., … Calkins, M. E. (2008). Abnormal auditory N100 amplitude: A heritable endophenotype in first-degree relatives of schizophrenia probands. *Biological Psychiatry*, *64*(12), 1051–1059. https://doi.org/10.1016/j.biopsych.2008.06.018

U.S. Department of Transportation, & Bureau of Transportation Statistics. (2020). *National Transportation Noise Map Documentation*. https://doi.org/10.21949/1520433

U.S. EPA (Environmental Protection Agency). (2015, June 3). *Clean Air Act Title IV - Noise Pollution* [Collections and Lists]. https://www.epa.gov/clean-air-act-overview/clean-air-act-title-iv-noise-pollution

van Kamp, I., & Davies, H. (2013). Noise and health in vulnerable groups: A review. *Noise and Health*, *15*(64), 153.

van Os, J., Kenis, G., & Rutten, B. P. F. (2010). The environment and schizophrenia. *Nature*, *468*(7321), Article 7321. https://doi.org/10.1038/nature09563

Ventura, J., Lukoff, D., Nuechterlein, K. H., Liberman, R. P., Green, M. F., & Shaner, A. (1993). Appendix 1: Brief Psychiatric Rating Scale (BPRS) Expanded Version (4.0): Scales, anchor points, and administration manual. *International Journal of Methods in Psychiatric Research*, *3*, 227–243.

Vinogradov, S., Fisher, M., & de Villers-Sidani, E. (2012). Cognitive training for impaired neural systems in neuropsychiatric illness. *Neuropsychopharmacology*, *37*(1), 43–76. https://doi.org/10.1038/npp.2011.251

Vita, A., Barlati, S., Ceraso, A., Nibbio, G., Ariu, C., Deste, G., & Wykes, T. (2021). Effectiveness, core Elements, and moderators of response of cognitive remediation for schizophrenia: A systematic review and meta-analysis of randomized clinical trials. *JAMA Psychiatry*, *78*(8), 848–858. https://doi.org/10.1001/jamapsychiatry.2021.0620

White, P. M., & Yee, C. M. (1997). Effects of attentional and stressor manipulations on the P50 gating response. *Psychophysiology*, *34*(6), 703–711. https://doi.org/10.1111/j.1469-8986.1997.tb02145.x

White, P. M., & Yee, C. M. (2006). P50 sensitivity to physical and psychological state influences. *Psychophysiology*, *43*(3), 320–328. https://doi.org/10.1111/j.1469-8986.2006.00408.x

Williams, T. J., Nuechterlein, K. H., Subotnik, K. L., & Yee, C. M. (2011). Distinct neural generators of sensory gating in schizophrenia. *Psychophysiology*, *48*(4), 470–478. https://doi.org/10.1111/j.1469-8986.2010.01119.x

Willmore, B. D. B., & King, A. J. (2023). Adaptation in auditory processing. *Physiological Reviews*, *103*(2), 1025–1058. https://doi.org/10.1152/physrev.00011.2022

World Health Organization (WHO). (2022). Environmental noise. In *Compendium of WHO and other UN guidance on health and environment, 2022 update*. World Health Organization. https://cdn.who.int/media/docs/default-source/who-compendium-on-health-and-environment/who_compendium_noise_01042022.pdf?sfvrsn=bc371498_3

Wright, B., Peters, E., Ettinger, U., Kuipers, E., & Kumari, V. (2014). Understanding noise stress-induced cognitive impairment in healthy adults and its implications for schizophrenia. *Noise and Health*, *16*(70), 166. https://doi.org/10.4103/1463-1741.134917

Wright, B., Peters, E., Ettinger, U., Kuipers, E., & Kumari, V. (2016). Effects of environmental noise on cognitive (dys)functions in schizophrenia: A pilot within-subjects experimental study. *Schizophrenia Research*, *173*(1), 101–108. https://doi.org/10.1016/j.schres.2016.03.017

Yee, C. M., Nuechterlein, K. H., Morris, S. E., & White, P. M. (1998). P50 suppression in recent-onset schizophrenia: Clinical correlates and risperidone effects. *Journal of Abnormal Psychology*, *107*(4), 691–698.

Yee, C. M., & White, P. M. (2001). Experimental modification of P50 suppression. *Psychophysiology*, *38*(3), 531–539. https://doi.org/10.1017/S0048577201981454

Yee, C. M., Williams, T. J., White, P. M., Nuechterlein, K. H., Ames, D., & Subotnik, K. L. (2010). Attentional modulation of the P50 suppression deficit in recent-onset and chronic

schizophrenia. *Journal of Abnormal Psychology*, *119*(1), 31–39. https://doi.org/10.1037/a0018265

Zimmermann, G., Favrod, J., Trieu, V. H., & Pomini, V. (2005). The effect of cognitive behavioral treatment on the positive symptoms of schizophrenia spectrum disorders: A meta-analysis. *Schizophrenia Research*, *77*(1), 1–9. https://doi.org/10.1016/j.schres.2005.02.018