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Neural Mechanisms of Motor Dysfunction in Individuals at Clinical High-Risk for Psychosis: Evidence for Impairments in Motor Activation

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Motor abnormalities are a core feature of psychotic disorders observed from the premorbid period through chronic illness, suggesting motor dysfunction may reflect the pathophysiology of psychosis. Electrophysiology research in schizophrenia suggests impaired motor activation and preparation may underlie these motor abnormalities. Despite behavioral studies suggesting similar motor dysfunction in those at clinical high-risk (CHR) for psychosis, there have been no studies examining neural mechanisms of motor dysfunction in the CHR period, where research can inform pathophysiological and risk models. The present study used the lateralized readiness potential (LRP), an event-related potential index of motor activation and preparation, to examine mechanisms of motor dysfunction in 42 CHR and 41 control participants (N = 83, 56% female). Response competition was manipulated to determine whether deficits are secondary to cognitive control impairments or reflect primary motor deficits. Behaviorally, CHR participants exhibited overall slower responses than controls. Further, relative to controls, CHR participants showed reduced activation of correct but not incorrect responses, reflected in blunted LRP amplitude under weak response competition and no difference in amplitude associated with the incorrect response under strong response competition. This pattern of results suggests individuals at CHR for psychosis exhibit primary motor deficits in activating and preparing behavioral responses and are contrary to a deficit in cognitive control. Further, blunted LRP amplitude was associated with worsening of negative symptoms at 12-month follow-up. Together, these findings are consistent with LRP studies in psychosis and implicate motor activation deficits as potential mechanisms of motor dysfunction in the high-risk period.

General Scientific Summary

Deficits in motor behavior are prevalent in individuals at risk for developing psychosis. This study supports the notion that for individuals at risk for psychosis, impairments in activating and preparing motor responses may underlie these deficits and predict the progression of symptoms. These findings suggest that deficits in motor activation and preparation may be present before illness onset and reflect a core feature of the illness.

Keywords: clinical high-risk for psychosis, event-related potential, lateralized readiness potential, motor, schizophrenia

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Deficits in goal-directed motor behavior, such as slowed movements and poor coordination, are core features of schizophrenia that have been considered important behavioral manifestations of the underlying pathophysiology of psychosis since the earliest conceptualizations of the disorder (Dickinson et al., 2007; Lee et al., 2013; Osborne, Walther, et al., 2020; Sponheim et al., 2010; Woodward et al., 2005). Despite several clinician-rated and behavioral studies suggesting that similar motor dysfunction is present in individuals that meet criteria for a clinical high-risk (CHR) syndrome (Dean & Mittal, 2015; Dean et al., 2018; Dickson et al., 2018; Dickson et al., 2020; Mittal et al., 2014; Mittal, Dean, et al., 2011; Mittal, Jalbrzikowski, et al., 2011), there has been no research examining the potential subprocesses, such as motor activation and preparation, underlying observed behavioral motor deficits. Indeed, research using the event-related potential (ERP) technique in schizophrenia has already started implicating motor activation and preparation impairments as potential mechanisms contributing to motor abnormalities in psychosis (Hughes et al., 2012; Kappenman et al., 2012, 2016; Kieffaber et al., 2007; Luck et al., 2009; Osborne, Kraus, et al., 2020; Van Voorhis et al., 2019), providing a pathway for examining this important domain in those meeting criteria for a CHR syndrome. Those that meet CHR syndrome criteria are considered at imminent risk for developing a psychotic disorder and have become a critical population for informing the field's understanding of the etiology and pathophysiology of psychosis. Considering that motor abnormalities are sensitive to illness severity and progression in the CHR period and are implicated in prominent etiological models of psychosis (Callaway et al., 2014; Howes & Kapur, 2009), identifying the mechanisms potentially underlying motor deficits in individuals that meet CHR criteria stands to inform the field's understanding of the pathophysiology and risk for psychotic disorders. However, there is currently no electrophysiology research examining whether motor activation and preparation deficits are present in individuals who meet criteria for a CHR syndrome or what mechanisms may contribute to potential deficits. To examine these open questions, the present study used ERPs to investigate electrophysiological deficits in motor activation and preparation in adolescents and young adults at CHR for psychosis.

The ERP technique is a noninvasive, high temporal resolution (i.e., millisecond range) method for examining the time-course of neural activity that occurs in response to sensory, cognitive, and motor events, such as perceiving a face or executing a motor behavior (Luck, 2014). An ERP arises from the simultaneous activation of neuronal populations consistently elicited by a given event and thus reflects the electrophysiological correlates of the corresponding sensory, cognitive, or motor processes involved in information processing (Woodman, 2010). Electrophysiology research in healthy individuals and patient populations has identified an ERP index of motor activation and preparation known as the lateralized readiness potential (LRP; de Jong et al., 1988; Gratton et al., 1988; Smulders & Miller, 2012). Consistent with the contralateral organization of the motor system, the LRP is elicited in tasks using lateralized motor responses (e.g., left-hand and right-hand responses) and is observed at electrodes over the motor cortex contralateral to the responding hand (de Jong et al., 1988; Eimer, 1998; Gratton et al., 1988). The LRP occurs a short time (~100–200 ms) before the execution of a behavioral response and reflects the point in time when the brain has begun to activate and prepare a selected action (Smulders & Miller, 2012). Indeed, there is strong evidence from single-unit recording and neuroimaging research suggesting the LRP is largely generated in the primary motor cortex (Coles, 1989; Eimer, 1998; Kristeva et al., 1991). Thus, the LRP reflects the lateralized activation of the motor cortices (i.e., motor activation) in preparation to execute motor actions (i.e., motor preparation) (de Jong et al., 1988; Kutas & Donchin, 1980). Because response activation occurs between when a stimulus is presented and a response is executed, the LRP can be observed both time-locked to the onset of the stimulus (i.e., stimulus-locked), providing information of unfolding response selection and preparation processes, or by looking at the response-locked LRP to see how the response is executed following the selection and preparation of the response. Across several studies, the LRP has been consistently shown to be reduced in amplitude and/or delayed in latency in patients with schizophrenia relative to controls, making the LRP an important marker of motor dysfunction in psychosis (Hughes et al., 2012; Kang et al., 2019; Kappenman et al., 2012, 2016; Karayanidis et al., 2006; Kieffaber et al., 2007; Luck et al., 2009; Mathalon et al., 2002; Van Voorhis et al., 2019).

There are several aspects of the LRP that make it particularly useful for identifying the specific mechanisms underlying motor dysfunction in psychosis. For example, the LRP is sensitive to experimental manipulations, such as the varying levels of response competition typical of cognitive control experiments in psychosis (Gratton et al., 1988). Specifically, in tasks with conditions of especially high response competition (e.g., Flankers, Simon, etc.), research has shown that the incorrect response is initially activated and prepared (e.g., the left-hand is activated when the right-hand is the correct response). This initial activation of the incorrect response is due to interference from distractors that map onto the incorrect response on that trial, requiring cognitive control processes to suppress incorrect or ineffective behavior in favor of intentionally selected, goal-directed action (Mathalon et al., 2002; Ridderinkhof et al., 2021). Initial activation of the incorrect response can be observed in the early portion of the LRP waveform as a positive deflection, known as the Gratton dip (Gratton et al., 1988; Kappenman et al., 2012), before the onset of the typical negative-going deflection that occurs prior to the execution of the correct response. As a result, the LRP waveform can be used to determine whether behavioral motor impairment typical of schizophrenia is due to a deficit in activating basic motor processes or is a secondary consequence of dysfunctional top-down cognitive control. For example, reduced LRP amplitude accompanied by reduced Gratton dip amplitude would implicate a basic motor deficit in activating and preparing behavioral responses. By contrast, reduced LRP amplitude and increased Gratton dip amplitude, would suggest that potential motor impairments are secondary consequences of deficits in cognitive control.

Research on the mechanisms of LRP blunting in patients with schizophrenia indicates that amplitude reductions are not due to difficulty with overcoming response competition (Kappenman et al., 2012; Mathalon et al., 2002), implicating a basic motor deficit rather than one secondary to cognitive control. Further, using a simple letter/digit discrimination task, it has been shown that LRP amplitude reductions in patients with schizophrenia reflect deficits specific to response selection and activation, rather than being a consequence of impairments in perception and stimulus categorization (Luck et al.,

2009), providing further support for a primary motor deficit. Together, these findings suggest that motor deficits in psychosis are due at least in part to difficulties in selecting, activating, and preparing responses. However, it is difficult to differentiate the extent to which deficits in these processes are related to the etiology and pathophysiology of the disorder from illness-related confounds known to contribute to motor deficits, such as medication use and illness duration (Peralta et al., 2010; Woodward et al., 2005). Research examining motor abnormalities using the CHR population can address this gap and improve our understanding of the pathogenesis of psychosis. Considering that motor dysfunction in schizophrenia is associated with pathophysiology and illness course (van Harten et al., 2017), as well as transition in those that meet CHR criteria (Callaway et al., 2014; Mittal et al., 2010), these are critical questions to examine.

Individuals at CHR for psychosis have not yet developed formal psychosis and thus are an ideal population to investigate the etiology and pathophysiology of the disorder in the absence of illness-related confounds. Individuals who meet criteria for a clinical high-risk syndrome experience attenuated positive symptoms (e.g., loosely held delusions, brief hallucinations) that are accompanied by a decline in psychosocial functioning and are considered at imminent risk for developing a psychotic disorder. Early evidence has suggested that upward of 35% of those that meet CHR criteria will convert to a psychotic disorder within a 2-year period (Cannon et al., 2008; Cannon et al., 2016; Dean et al., 2014); however, more recent research indicates that transition rates may be closer to 10% to 20% (Addington et al., 2017; Perkins et al., 2015; Seidman et al., 2016; Salazar de Pablo et al., 2021). To date, evidence from clinician ratings of overt motor behavior, such as neurological soft signs and involuntary movements, provide initial evidence for the presence of motor abnormalities in the high-risk period of the illness (Mittal et al., 2008, 2010, 2014). Those at CHR for psychosis also exhibit impaired performance on writing, pegboard, and tapping paradigms that is similar to those observed in formal psychosis (Damme et al., 2020; Damme et al., 2021; Dean et al., 2013; Dickson et al., 2018, 2020; Gallucci et al., 1997; Müller et al., 2002). Whereas neuroimaging work has begun to inform brain-behavior relationships of motor abnormalities in the high-risk period (Dean et al., 2020; Mittal et al., 2017; Schiffman, 2017), both overt behavior and neuroimaging methods lack the temporal resolution required to assess quickly unfolding motor subprocesses that may contribute to observed behavioral motor deficits. Given strong evidence from LRP work for motor activation and preparation deficits in schizophrenia (Hughes et al., 2012; Kappenman et al., 2012, 2016; Karayanidis et al., 2006; Luck et al., 2009; Mathalon et al., 2002; Van Voorhis et al., 2019), using the ERP technique to examine if similar impairments are present in individuals at CHR will aid efforts to determine whether observed deficits in schizophrenia are a consequence of the illness or part of the risk for the disorder and/or illness pathophysiology.

The Present Study

In the present study, we examined whether deficits in motor activation and preparation are present in those at CHR for psychosis. Specifically, we used the ERP technique to measure mechanisms of motor dysfunction in those at CHR for psychosis and healthy controls using the LRP. Similar to past work in schizophrenia (Kappenman et al., 2012; Mathalon et al., 2002), we examined whether potential motor activation and preparation deficits are primarily attributable to basic motor processes or are secondary consequences of dysfunctional top-down cognitive control processes. This was accomplished by using a well-studied experimental paradigm, the Flankers task (Eriksen & Eriksen, 1974), which has been consistently shown to induce response competition, as evidenced by increased reaction times and the presence of a Gratton dip in the ERP waveform on trials with strong response competition (i.e., incongruent flankers; Gratton et al., 1988; Ridderinkhof et al., 2021).

If CHR participants exhibit a deficit in cognitive control in the present study, we would expect to see a greater reduction in LRP amplitude in CHR participants compared with controls, particularly in the strong response competition condition (i.e., incongruent flankers trials), in which increased cognitive control is needed to overcome activation of the incorrect response. Similarly, we would expect to see CHR participants exhibit a larger Gratton dip compared with controls, reflecting an inability of CHR participants to exert control to inhibit initial activation of the incorrect response. If instead a basic motor deficit is present in CHR participants, we would expect to see an overall reduction in both the amplitude of the Gratton dip and the amplitude of the LRP in CHR participants irrespective of response competition, reflecting an overall difficulty in activating responses. We predicted that, similar to patients with schizophrenia (Kappenman et al., 2012; Mathalon et al., 2002), individuals at CHR for psychosis would exhibit an overall deficit of motor function, as evidenced by a reduced LRP amplitude and decreased activation of the incorrect response in CHR. Because there is robust evidence for relationships between motor dysfunction and clinical characteristics (i.e., negative symptoms and functioning) across the schizophrenia spectrum (Cuesta et al., 2018; Mittal & Walker, 2007; Walther & Mittal, 2017), we also conducted exploratory analyses examining potential relationships between reaction time (RT) and ERP measures, baseline symptoms and functioning, and worsening of symptoms and functioning over a 12-month period.

Method

Participants

Data for the present study were obtained from 42 healthy control (HC) and 42 individuals at CHR for psychosis at the Adolescent Development and Preventative Treatment (ADAPT) program at Northwestern University (see Table 1 for demographics/clinical characteristics). Exclusion criteria for both groups included any history of significant head injury, intellectual disability or neurological disorder, or any past or current psychotic disorder (e.g., schizophrenia). For HCs, the presence of a psychotic disorder in a first-degree relative was an additional exclusionary criterion. Further, in our EEG studies, we typically reject participants with greater than 50% of trials rejected for EEG artifacts; no participants exceeded this threshold in the present study. Participants were also excluded from analyses if task accuracy was lower than 65%; one HC participant was excluded for this reason. Thus, the final sample consisted of 41 HC and 42 CHR participants included in analyses (final $N = 83$; 15–30 years old, M age = 20.81, SD age = 2.78, 56% female). To be included in the CHR group, participants were required to meet the Criteria of Prodromal Syndromes (COPS; McGlashan et al., 2010) for a psychosis-risk

Table 1
Demographics and Clinical Characteristics With Group Comparisons

Demographic/Characteristic	CHR	HC	Statistic	*p*
Age	20.52 (2.73)	21.02 (2.82)	$t(81) = -0.82$	ns
Gender				
Male	21	16		
Female	21	25	$\chi^2(1) = 1.01$	ns
Education (yr.)	13.87 (2.00)	14.29 (2.30)	$t(80) = -0.88$	ns
Parent education (yr.)	15.10 (3.73)	16.12 (2.96)	$t(81) = -1.39$	ns
Baseline				
Positive symptoms	10.76 (3.50)			
Negative symptoms	6.71 (4.90)			
GFS:S	7.63 (1.37)			
GFS:R	7.94 (1.28)			
12-month follow-up				
Positive symptoms	8.29 (3.26)			
Negative symptoms	6.44 (5.29)			
GFS:S	7.69 (1.38)			
GFS:R	7.81 (1.49)			

Note. Descriptive statistics reflect means and standard deviations (in parentheses). Inferential statistics reflect tests of group differences from individuals included in final analyses. CHR = clinical high-risk; HC = healthy controls; GFS:S = Global Functioning Scale: Social; GFS:R = Global Functioning Scale: Role; ns = nonsignificant. Years of education was unavailable for one CHR participant. Positive and negative symptoms were quantified using the Structure Clinical Interview for Psychosis Risk Syndromes (SIPS).

syndrome (i.e., clinical high-risk) which included one or more of the following: (a) progression or recent onset of attenuated positive symptoms, (b) the presence of a first-degree relative with a psychotic disorder accompanied by a recent decline in global functioning, or (c) a decline in global functioning with the presence of schizotypal personality disorder (McGlashan et al., 2010). Participants were recruited via Craigslist, community professional referrals, and advertisement postings locally and throughout the greater Chicago area. Informed consent was obtained in accordance with the protocol approved by the Institutional Review Board. Assent was obtained for individuals younger than 18 with informed consent obtained from their legal guardian.

Clinical Interviews and Functioning Assessment

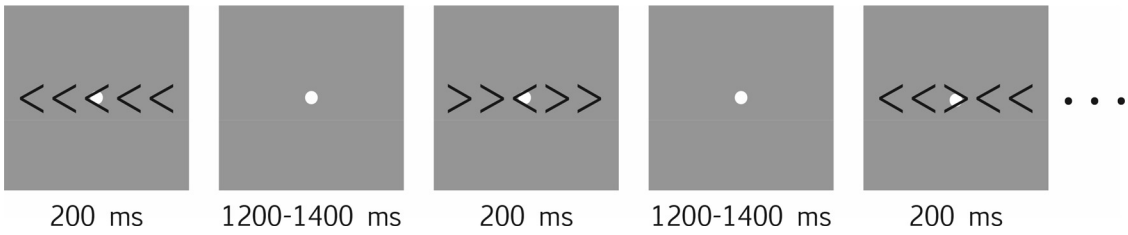
The Structured Interview for Psychosis Risk Syndromes (SIPS; McGlashan et al., 2010; Miller et al., 1999) was administered to diagnose a CHR syndrome. The SIPS assesses several different dimensions of attenuated positive and negative symptomology. Specifically, positive symptomology comprises dimensions reflecting unusual thought content, suspiciousness, perceptual abnormalities, grandiosity, and disorganized communication. Negative symptom dimensions include social anhedonia, avolition, ideational richness, emotional expressiveness, blunted affect, and occupational functioning. All symptom dimensions are rated on 0 to 6 scales with positive symptom ratings ranging from *absent* (0) to *psychotic* (6) and negative symptom dimensions using an *absent* (0) to *extreme* (6) scale. Sum scores were used to quantify positive and negative symptoms at baseline and 12-month follow-up. Social and role functioning were measured using two scales explicitly designed for CHR populations: the Global Functioning Scale: Social (GFS-S; Auther et al., 2006) and Global Functioning Scale: Role (GFS-R; Niendam et al., 2006). Scores on both scales range from 1 to 10. A score of 1 on the GFS-S indicates extreme social isolation (e.g., no friends or contact with family), whereas a score of 10 reflects superior interpersonal functioning (e.g., multiple satisfying close and casual interpersonal relationships). On the GFS-R, a score of 1 indicates extreme role dysfunction (e.g., on disability or equivalent nonindependent status) and a score of 10 represents superior role functioning (e.g., superior performance in competitive school or work placement). These scales were developed to be used with adolescents and young adults and have been shown to be valid and reliable in CHR populations (Cornblatt et al., 2007). In addition, the Structured Clinical Interview for DSM-V Disorders (SCID; American Psychiatric Association, 2013) was administered to rule out a psychotic disorder and to note the occurrence of any comorbid conditions at both baseline and 12-month follow-up.

Task Design

The LRP was elicited using the ERP CORE (Compendium of Open Resources and Experiments; Kappenman et al., 2021) arrowhead variant of the Eriksen flankers task (Eriksen & Eriksen, 1974). This task uses highly learned stimulus response mappings (e.g., < for left; > for right), which affords the ability to examine response competition and activation while minimizing demands on cognitive processes such as working memory and learning. The experiment was displayed on an LCD monitor using Presentation software (Neurobehavioral Systems, Inc., Berkeley, CA). Participants were required to identify the direction of a central arrowhead that was flanked by a horizontally aligned array of either congruent (e.g., < < < < <) or incongruent (e.g., < < > < <) arrowheads. There is an extensive literature demonstrating that the presence of incongruent flankers induces strong response competition (Ridderinkhof et al., 2021). On each trial, an arrowhead array was displayed for 200 ms, centered on a continuously visible fixation point, followed by an interstimulus interval (ISI) of 1200–1400 ms (see Figure 1 for a trial sequence example). Participants were instructed to identify the direction of the central arrowhead by making left-hand responses for left-facing arrows and right-hand responses for right-facing arrows. Responses were made with left/right index fingers using a Logitech Precision gamepad.

All arrowheads subtended 1° horizontal and 1° vertical visual angle from a viewing distance of 70 cm. The experiment consisted

Figure 1
Example Trials of the Flankers Task



of 10 blocks of 40 trials each, with an equal number of trials across the four combinations of arrow direction (i.e., left/right) and flanker type (i.e., congruent/incongruent) randomly interspersed throughout the blocks, resulting in 400 total trials with 100 trials per trial type. In addition, feedback was provided on a block-by-block basis to maintain a consistent tradeoff between speed and accuracy throughout the task. Specifically, if participants missed less than 10% of trials in a block, they were presented with the message "Try to respond a bit faster." If participants missed more than 20% of trials in a block, they were presented with the message "Try to respond more accurately." If participants missed between 10% and 20% of trials in a block, they were presented with the message "Good job!"

EEG Recording and Processing Procedures

The electroencephalogram (EEG) was recorded from 58 passive Ag/AgCl electrodes mounted in an elastic cap positioned according to the International 10–20 System (Jasper, 1958) within an electromagnetically shielded booth. A subset of these electrodes was selected for further processing (Fp1, Fpz, Fp2, F3, Fz, F4, F7, F8, FC3, FCz, FC4, C3, Cz, C4, C5, C6, CPz, P3, Pz, P4, P7, P8, PO3, POz, PO4, PO7, PO8, O1, Oz, O2). The vertical electrooculogram (VEOG) was recorded from electrodes placed above and below the left eye, and the horizontal electrooculogram (HEOG) was recorded from electrodes placed beside each eye near the external canthi. Recordings were made using an online left mastoid reference and then rereferenced offline to the average of the left and right mastoids. Data were amplified using a Neuroscan Synamps RT amplifier with 24-bit resolution at DC with a 100 Hz antialiasing filter digitized at 500 Hz. All impedances were kept below 5 kΩ.

Signal processing was conducted offline in MATLAB using EEGLAB (Delorme & Makeig, 2004) and ERPLAB toolboxes (Lopez-Calderon & Luck, 2014). The DC offsets were removed, and then the data were high-pass filtered (noncausal Butterworth impulse response function, half-amplitude cut-off at .1 Hz, 12 dB/octave roll-off). Independent components analysis (ICA; Jung et al., 2000) was then performed on each participant's continuous data and components consistent with ocular artifacts were removed. The ICA-corrected continuous data were segmented between −200 and 800 ms relative to stimulus onset for the stimulus-locked averages (baseline corrected using the −200 to 0 ms prestimulus interval) and segmented between −800 to 200 ms relative to the onset of the response for the response-locked averages (baseline corrected between −800 and −600 ms within the preresponse interval). Channels with excessive noise were identified through visual inspection and interpolated using spherical interpolation. Individual segments were then flagged and rejected using a semiautomated procedure, in which automated ERPLAB algorithms were applied using individualized thresholds for each participant based on that participant's data (justification for individualized thresholds can be found in Luck, 2014). Specifically, trials were excluded with large voltage shifts in any channel. Further, because ICA does not always perfectly remove eye movement artifacts, we also discarded trials with large eye movements (greater than 4° of visual angle) present in the ICA corrected HEOG. Data segments corresponding to trials with incorrect behavioral responses or reaction times less than 200 ms or greater than 1,000 ms were excluded from ERP waveform averages. All signal processing and artifact rejection procedures were performed by an individual blind to group membership.

Behavioral and ERP Measurement Procedures

Median RTs and mean accuracy (percent correct) were quantified separately for each condition and group. Consistent with past research and field standards (Eimer, 1998; Kappenman et al., 2012; Kappenman et al., 2016; Luck et al., 2009; Mathalon et al., 2002; Smulders & Miller, 2012; Verleger et al., 2010), the LRP was quantified from the contralateral-minus-ipsilateral difference waveform derived from lateral central sites C3 and C4. Specifically, the LRP was computed for each participant by first creating separate waveforms for left- and right-hand responses for the hemisphere that was contralateral to the responding hand and the hemisphere that was ipsilateral to the responding hand. Contralateral and ipsilateral waveforms were then averaged together across left- and right-hand responses, resulting in average contralateral and ipsilateral waveforms. A contralateral-minus-ipsilateral difference waveform was then created to isolate the LRP (see Smulders & Miller, 2012). The presence of an opposite-polarity Gratton dip in the strong response competition condition (i.e., incongruent flankers) made it difficult to characterize the LRP within a single time window. Thus, in line with Kappenman et al. (2012), stimulus- and response-locked LRP mean amplitudes were measured in consecutive 100 ms intervals across a measurement window of 200 to 500 ms after stimulus onset and between −300 and 0 ms relative to the response. As expected, the corresponding stimulus-locked and response-locked waveforms are correlated with one another (*r*s for negative deflection LRP from .41 to .77; *r*s for Gratton dip from .32 to .48).

Both the ERP quantification and analytic approach were chosen a priori based off prior research (Kappenman et al., 2012) to avoid bias that might result from choosing electrode sites and measurement windows on the basis of the observed data (Keil et al., 2014;

Luck, 2014). However, because this approach splits the response-locked Gratton dip component into two different measurement windows, and also makes it difficult to determine if observed mean amplitude effects in the stimulus-locked waveforms are due to group differences in amplitude or group differences in latency, we also conducted sensitivity analyses to address these limitations. Specifically, we used a peak amplitude approach that provides a single measure of the response-locked Gratton dip amplitude and is less sensitive to differences in latency across groups and conditions (see online supplemental materials for details).

Statistical Analysis Approach

Independent *t* tests and chi-square tests were employed to examine group differences in demographic variables. A series of 2 (Group: CHR vs. HC) × 2 (Condition: Weak vs. Strong Response Competition) repeated measures ANOVAs were used to examine group effects and interactions. Pearson correlations were used to examine associations between RT and ERP measures and baseline symptoms and functioning. To examine relationships between RT and ERP measures and worsening of symptoms and functioning, we used a series of multiple regression models predicting change in positive symptoms, negative symptoms, and social and role functioning at 12-month follow-up from both behavioral and ERP measures while controlling for baseline symptoms or functioning for the corresponding outcome variable. Change scores were computed by subtracting baseline positive and negative symptoms and baseline social and role functioning from 12-month follow-up positive and negative symptoms and 12-month social and role functioning, respectively. Longitudinal analyses were conducted on a subset of 33 CHR participants with 12-month follow-up symptom assessment, and for 28 CHR participants with 12-month follow-up functioning assessment. Two-tailed tests with an alpha level of .05 were used for all statistical tests. Estimates of effect size with 95% confidence intervals (CI) are provided for relevant *t* statistics and 90% CIs are provided for *F* statistics. Note, in line with current recommendations (Lakens, 2013; Smithson, 2001), 90% CIs are provided for *F* test effect sizes because *F* tests are inherently one-sided and using a 95% CI may result in 0 being added in the CI around the effect size, even for statistically significant *F* tests, whereas 90% CIs always exclude 0 when the test is statistically significant (Lakens, 2013).

Results

There were no significant group differences in regard to age, sex, education, or parent education (a proxy for socioeconomic status; see Table 1 for statistics). Because one CHR participant was receiving neuroleptic treatment during the study, sensitivity analyses were conducted with this participant excluded. Results did not change with removal of this participant, and thus findings with the full sample are reported. In addition, findings from the peak amplitude sensitivity analyses were consistent with the a priori mean amplitude approach suggesting that mean amplitude findings are not being driven by differences in latency across groups and conditions (see online supplemental materials for statistics).

Behavior

Reaction Time

Median RTs and mean accuracy for congruent and incongruent flanker conditions are reported in Table 2. Overall, participants were slower on trials with strong response competition (i.e., incongruent flankers) compared with weak response competition (i.e., congruent flankers), leading to a significant main effect of condition, $F(1, 81) = 733.38$, $p < .001$, $\eta_p^2 = .90$. Furthermore, CHR participants also exhibited overall slower responses compared with HCs (approximately 17 ms slower), as indicated by a significant main effect of group, $F(1, 81) = 4.58$, $p = .035$, $\eta_p^2 = .05$. There was no significant Group × Condition interaction, $F(1, 81) = .03$, $p = .88$, $\eta_p^2 = .00$.

Accuracy

Regarding accuracy, participants were more accurate in the weak response competition condition (i.e., congruent flankers) than in the strong response competition condition (i.e., incongruent flankers), leading to a significant main effect of condition, $F(1, 81) = 311.65$, $p < .001$, $\eta_p^2 = .79$. Specifically, both the CHR group and HC group were approximately 18% more accurate when making responses in the presence of weak response competition compared with strong response competition. Overall, accuracy was similar for both the CHR and HC group, leading to a nonsignificant main effect of group, $F(1, 81) = .34$, $p = .56$, $\eta_p^2 = .00$. There was no Group × Condition interaction, $F(1, 81) = .46$, $p = .50$, $\eta_p^2 = .01$.

ERP Waveforms

Contralateral-minus-ipsilateral grand average difference waveforms (i.e., LRP) and associated topographical maps are shown in Figures 2 and 3. The left panel of each figure shows the stimulus-locked waveforms, and the right panel of each figure shows the response-locked waveforms. The same data are depicted in the figures, with the waveforms overlaid for each group separately for each condition in Figure 2, and the waveforms overlaid for each condition separately for each group in Figure 3 The LRP mean amplitude measures are summarized in Table 2 and depicted in Figure 4.

Stimulus-Locked LRP

In the weak response competition condition, a negative deflection was observed from approximately 200 to 500 ms, with a smaller magnitude LRP in the CHR participants compared with the controls (Figure 2A). In the strong response competition, a Gratton dip (positive deflection) was observed in the early portion of the waveform in both groups, reflecting activation of the incorrect response, followed by a negative deflection until approximately 550 ms, reflecting subsequent activation of the correct response (Figure 2C). As mentioned above, the presence of the opposite-polarity Gratton dip at the beginning of the LRP in the strong response competition made it difficult to characterize the LRP with a single time window. Thus, to separately analyze the Gratton dip period from the negative deflection LRP, we computed 2 (Group) × 2 (Condition) repeated measures ANOVAs for each of the 100-ms time periods.

200–300 ms Time Window. The Gratton dip was observed in the strong response competition condition (i.e., incongruent flankers) but not the weak response competition condition (i.e., congruent flankers; Figure 3A and 3C), leading to a significant main effect of

Table 2

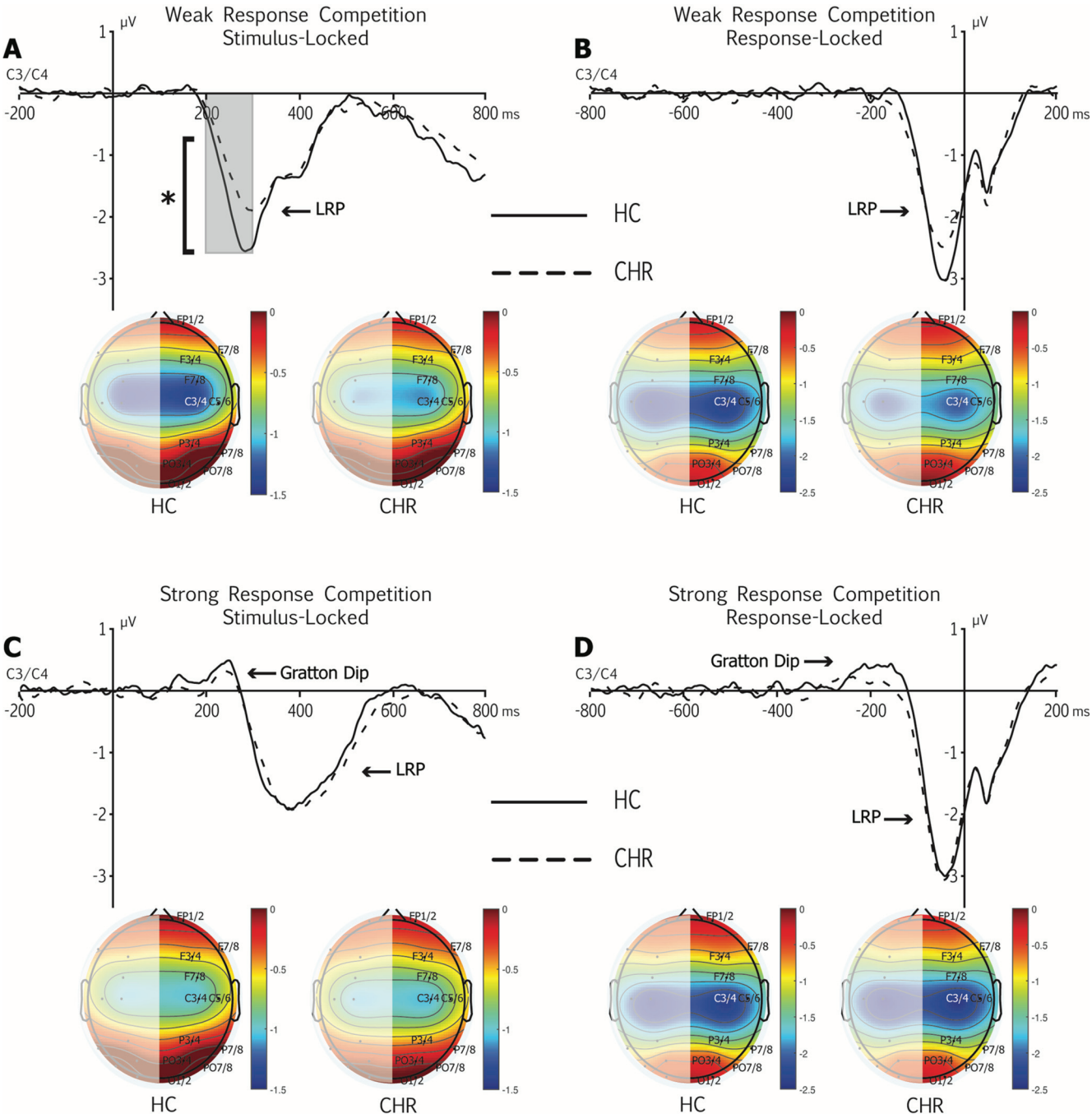
Descriptive and Inferential Statistics for Behavioral and Stimulus- and Response-Locked LRP Measures

		CHR		HC		Statistics		
Measure	Time window (ms)	Congruent	Incongruent	Congruent	Incongruent	Group (*df* = 1.81)	Condition (*df* = 1.81)	Group × Condition (*df* = 1.81)
Behavioral								
Median RT	—	356.79 (36.96)	423.98 (41.87)	340.39 (30.33)	406.81 (39.51)	**$F = 4.58$; $p = .035$; $\eta_p^2 = .05$; 90% CI [.002, .15]**	**$F = 733.38$; $p < .001$; $\eta_p^2 = .90$; 90% CI [.87, .92]**	$F = 0.03$; $p = .88$; $\eta_p^2 = .00$; 90% CI [.00, .02]
Accuracy	—	95.70 (5.13)	78.28 (8.10)	97.05 (2.20)	78.24 (9.82)	$F = 0.34$; $p = .56$; $\eta_p^2 = .00$; 90% CI [.00, .06]	**$F = 311.65$; $p < .001$; $\eta_p^2 = .79$; 90% CI [.73, .78]**	$F = 0.46$; $p = .50$; $\eta_p^2 = .01$; 90% CI [.00, .06]
LRP Amplitude								
Stimulus-locked	200–300	−1.20 (0.69)	0.03 (0.45)	−1.71 (1.12)	0.13 (0.66)	$F = 2.59$; $p = .11$; $\eta_p^2 = .03$; 90% CI [.00, .11]	**$F = 190.04$; $p < .001$; $\eta_p^2 = .70$; 90% CI [.61, .76]**	**$F = 7.14$; $p < .01$; $\eta_p^2 = .08$; 90% CI [.01, .19]**
	300–400	−1.51 (1.03)	−1.58 (0.99)	−1.62 (1.44)	−1.67 (1.16)	$F = 0.21$; $p = .65$; $\eta_p^2 = .00$; 90% CI [.00, .05]	$F = 0.19$; $p = .67$; $\eta_p^2 = .00$; 90% CI [.00, .05]	$F = .004$; $p = .95$; $\eta_p^2 = .00$; 90% CI [.00, .00]
	400–500	−0.59 (1.24)	−1.58 (0.98)	−0.60 (1.32)	−1.46 (1.34)	$F = 0.06$; $p = .82$; $\eta_p^2 = .00$; 90% CI [.00, .03]	**$F = 60.58$; $p < .001$; $\eta_p^2 = .43$; 90% CI [.29, .53]**	$F = 0.30$; $p = .58$; $\eta_p^2 = .00$; 90% CI [.00, .05]
Response-locked	−300 – −200	0.01 (0.40)	0.17 (0.50)	0.02 (0.43)	0.20 (0.44)	$F = 0.11$; $p = .74$; $\eta_p^2 = .00$; 90% CI [.00, .04]	**$F = 5.93$; $p = .017$; $\eta_p^2 = .07$; 90% CI [.01, .17]**	$F = 0.01$; $p = .91$; $\eta_p^2 = .00$; 90% CI [.00, .01]
	−200 – −100	−0.36 (0.58)	−0.11 (0.51)	−0.19 (0.05)	0.20 (0.64)	**$F = 5.77$; $p = .019$; $\eta_p^2 = .07$; 90% CI [.01, .17]**	**$F = 20.67$; $p < .001$; $\eta_p^2 = .20$; 90% CI [.09, .32]**	$F = 1.02$; $p = .32$; $\eta_p^2 = .01$; 90% CI [.00, .08]
	−100–0	−2.08 (0.86)	−2.43 (1.02)	−2.36 (1.39)	−2.35 (1.4)	$F = 0.18$; $p = .67$; $\eta_p^2 = .00$; 90% CI [.00, .05]	**$F = 5.71$; $p = .019$; $\eta_p^2 = .07$; 90% CI [.01, .17]**	**$F = 6.31$; $p = .014$; $\eta_p^2 = .07$; 90% CI [.01, .17]**

Note. Descriptive statistics reflect means and standard deviations (in parentheses). Significant findings are bolded. CHR = clinical high-risk; HC = healthy controls; RT = reaction time; LRP = lateralized readiness potential; CI = confidence interval. LRP amplitude reflects mean amplitude in microvolts (μVs) at C3/C4. Accuracy values reflect percent correct.

Figure 2

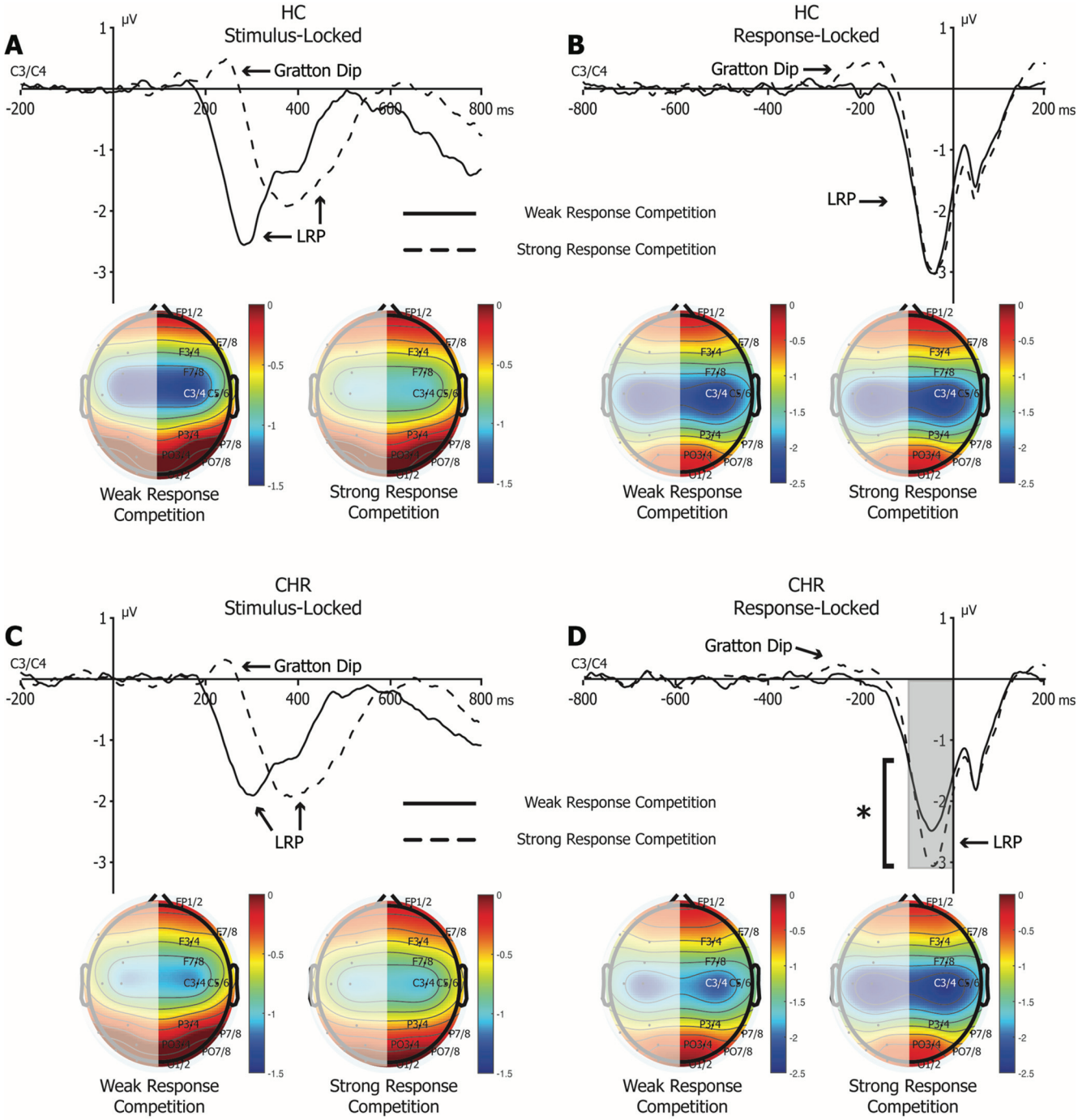
Grand Average Lateralized Readiness Potential (LRP) Waveform Between-Group Comparisons Across Conditions



Note. CHR = clinical high-risk; HC = healthy controls. Event-related potential (ERP) waveforms reflect grand average difference waveforms (contralateral minus ipsilateral) averaged over C3 and C4 electrode sites. The shaded region depicted in panel A reflects a significant between-group difference in the weak response competition condition. Topographical maps reflect grand average of the mean amplitude for the difference waveforms (contralateral minus ipsilateral) across the full time window of each component (stimulus-locked 200–500 ms; response-locked −300–0) for each group and condition. Because the LRP data are collapsed across hemispheres, the data for the topographical maps are presented mirrored in the left and right hemispheres. * $p = .016$. See the online article for the color version of this figure.

Figure 3

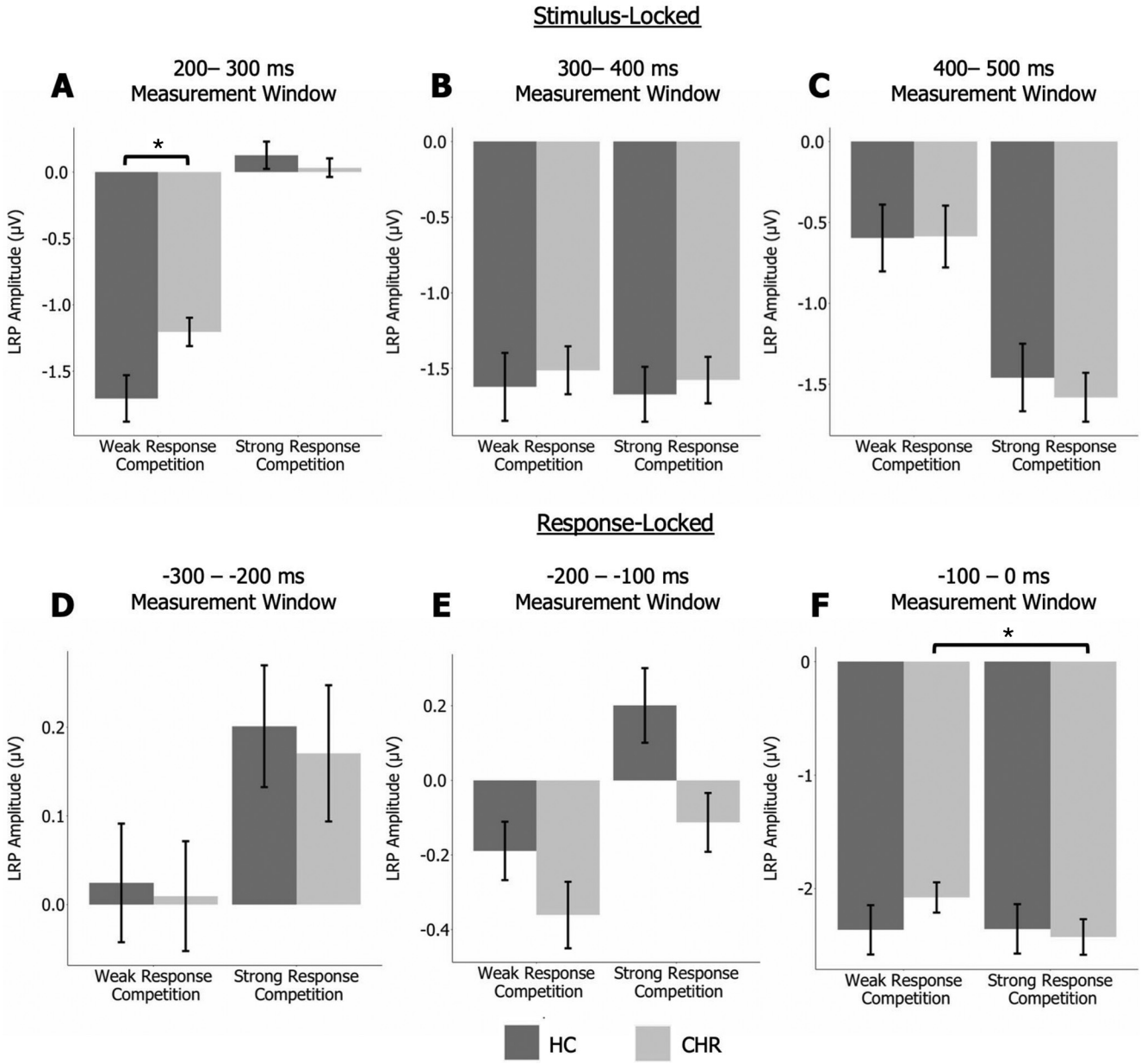
Grand Average Lateralized Readiness Potential (LRP) Waveforms Within-Group Comparisons Across Conditions



Note. CHR = clinical high-risk; HC = healthy controls. Event-related potential (ERP) waveforms reflect grand average difference waveforms (contralateral minus ipsilateral) averaged over C3 and C4 electrode sites. The shaded region depicted in panel D reflects a significant within-group difference between conditions in the CHR group. Topographical maps reflect grand average of the mean amplitude for the difference waveforms (contralateral minus ipsilateral) across the full time window of each component (stimulus-locked 200–500 ms; response-locked −300–0) for each group and condition. Because the LRP data are collapsed across hemispheres, the data for the topographical maps are presented mirrored in the left and right hemispheres. * $p = .003$. See the online article for the color version of this figure.

Figure 4

Bar Graphs Depicting Mean Lateralized Readiness Potential (LRP) Amplitudes for the CHR and HC Groups



Note. CHR = clinical high-risk; HC = healthy controls. LRP amplitude reflects mean amplitude within the respective time window from the difference waveforms (contralateral minus ipsilateral) averaged over C3 and C4 electrode sites. The asterisk in panel A reflects a between group difference in the weak response competition condition, which is depicted in the shaded region Figure 2A. The asterisk in panel F reflects a within group difference between the weak response competition and strong response competition conditions in the CHR group, which is depicted in the shaded region Figure 3D.
For panel A, * $p = .016$. For panel F, * $p = .003$.

condition in the 200 to 300 ms time window, $F(1, 81) = 190.04$, $p < .001$, $\eta_p^2 = .70$. Although this same pattern was observed for both groups, the negative deflection LRP in the weak response competition condition was larger in HCs than the CHR participants, leading to a significant Group × Condition interaction, $F(1, 81) = 7.14$, $p = .009$, $\eta_p^2 = .08$. Specifically, follow-up analyses revealed that the negative deflection LRP observed in the weak response competition condition (where no Gratton dip was present) showed a significantly smaller amplitude in the CHR participants compared with controls (Figure 2A shaded region; Figure 4A), reflecting a decreased activation of the correct response, $t(81) = 2.46$, $p = .016$, $d = .55$. By contrast, Gratton dip amplitude in the strong response competition condition (i.e., incongruent flankers) did not differ statistically between groups, indicating there was no significant difference in the activation of the incorrect response between HC and CHR participants, $t(81) = -.76$, $p = .45$, $d = .18$. There was not main effect of group, $F(1, 81) = 2.59$, $p = .11$, $\eta_p^2 = .03$.

300–400 and 400–500 ms Time Windows. Although no main effects or interactions were observed in the middle portion (300 to 400 ms) of the LRP waveform, the initial activation of the incorrect response in the strong response competition condition led to a later overall completion of the LRP compared with the weak response competition condition (see Figure 3A and 3C). This was reflected in a larger LRP amplitude in the strong response competition in the 400 to 500 ms time window, leading to a significant main effect of condition, $F(1, 81) = 60.58$, $p < .001$, $\eta_p^2 = .43$. No other main effects or interactions were observed with the stimulus-locked waveforms (see Table 2 for statistics).

Response-Locked LRP

As in the stimulus-locked data, an initial Gratton dip was present in both groups in the strong response competition condition (Figure 2D), reflecting an initial activation of the incorrect response, followed by a subsequent negative deflection, reflecting activation of the correct response. In the weak response competition condition, only the negative deflection was observed (Figure 2B).

−300 to −200 ms Time Window. Similar to the stimulus-locked waveforms, the Gratton dip observed in the strong response competition condition (i.e., incongruent flankers) was not present in the weak response competition condition (i.e., congruent flankers; Figure 2B and 2D), which led to a significant main effect of condition within the −300 to −200 ms measurement window, $F(1, 81) = 5.93$, $p = .017$, $\eta_p^2 = .07$. This effect was of similar magnitude in both groups, and the group main effect and Group × Condition interaction were not statistically significant (see Table 2).

−200 to −100 ms Time Window. In the subsequent −200 to −100 ms time window, in which the Gratton dip was still present in the strong response competition condition but not the weak response competition condition, a similar main effect of condition was observed, $F(1, 81) = 20.67$, $p < .001$, $\eta_p^2 = .20$. In addition, in this later time window, the overall LRP amplitude across conditions was reduced in the CHR participants compared with HCs, leading to a significant main effect of group, $F(1, 81) = 5.77$, $p = .019$, $\eta_p^2 = .07$. The Group × Condition interaction in the −200 to −100 ms window was not statistically significant, $F(1, 81) = 1.02$, $p = .32$, $\eta_p^2 = .01$.

−100 to 0 ms Time Window. In the −100 to 0 ms window, in which a negative deflection LRP was observed in both response competition conditions (Figure 3B and 3D), there was a significant main effect of condition, $F(1, 81) = 5.71$, $p = .019$, $\eta_p^2 = .07$, and a significant Group × Condition interaction, $F(1, 81) = 6.31$, $p = .014$, $\eta_p^2 = .07$; the main effect of group did not reach significance, $F(1, 81) = .18$, $p = .67$, $\eta_p^2 = .00$. Follow-up analyses revealed the Group × Condition interaction was driven by a difference in amplitude between the strong and weak response competition conditions in the CHR group that was not present in the HCs. Specifically, the CHR group exhibited a reduced LRP amplitude in the weak response competition condition (i.e., congruent flankers) relative to the strong response competition condition (i.e., incongruent flankers; Figure 3D shaded region; Figure 4F), $t(41) = 3.15$, $p = .003$, $d = .50$. By contrast, healthy controls showed no difference in LRP amplitude between conditions (Figure 3B), $t(40) = -.10$, $p = .92$, $d = .02$. LRP amplitude did not differ statistically between groups in either the weak response, $t(81) = 1.13$, $p = .26$, $d = .24$, or strong response competition condition, $t(81) = -.27$, $p = .79$, $d = .07$.

Reaction Time, ERP Measures, and Symptom and Functioning Associations

Results from the exploratory correlation and multiple regression analyses between RT and ERP measures and positive symptoms, negative symptoms, and social and role functioning are provided in Tables 3 and 4, respectively. To avoid inflating the experiment-wise type I error rate, examination of associations between RT and ERP measures and positive symptoms, negative symptoms, and social and role functioning were limited to the most theoretically relevant behavioral measures and time windows with either between- or within-group differences (i.e., Overall RT collapsed across condition, shaded region Figure 2A, and shaded region Figure 3D).

Reaction Time

There was not a significant Group × Condition interaction for RT measures, but there was a main effect of group, thus we focused on relationships between overall RT (collapsed across conditions) and baseline and 12-month follow-up symptoms and functioning. Regarding baseline symptoms and functioning, although the direction and magnitude of correlations suggest that there may be small to medium sized effects for longer overall RTs being associated with more severe baseline negative symptoms ($r = .20$) and worse social ($r = -.14$) and role functioning ($r = -.28$), these correlations were not statistically significant ($ps > .11$). By contrast, longer overall RTs were associated with worsening of negative symptoms at 12-month follow-up ($\beta = .32$, $p = .029$), but not worsening of

Table 3
Correlations Between LRP and RT Measures and Baseline Symptoms and Functioning Within the CHR Group

Measure	Time window (ms)	Response competition condition	Positive symptoms	Negative symptoms	GFS:S	GFS:R
Behavioral						
Median RT		Overall RT	.04	.20	−.14	−.28
LRP amplitude						
Stimulus-locked	200−300	Weak	.09	.12	−.14	−.21
Response-locked	−100−0	Weak	.05	.07	.15	−.02
		Strong	.05	.07	.10	.06

Note. Correlations were limited to overall RT (i.e., collapsed across conditions) and the most theoretically relevant time windows with either between- or within-group differences (i.e., shaded region Figure 2A and shaded region Figure 3D). LRP amplitudes reflect time windows in which there was a negative deflection associated with the correct response. CHR = clinical high-risk; RT = reaction time; LRP = lateralized readiness potential; GFS:S = Global Functioning Scale: Social; GFS:R = Global Functioning Scale: Role. *df* = 40 for symptoms and 33 for functioning.

Table 4
Multiple Linear Regression Results for LRP and RT Measures Predicting Symptoms and Functioning at Follow-Up Within the CHR Group

Measure	Time window (ms)	Response competition condition	Positive symptoms	Negative symptoms	GFS:S	GFS:R
Behavioral						
Median RT		Overall RT	β = .02 95% CI [−.28, .31]	**β = .32* 95% CI [.03, .61]**	β = −.21 95% CI [−.54, .12]	β = −.03 95% CI [−.45, .23]
LRP amplitude						
Stimulus-locked	200–300	Weak	β = .03 95% CI [−.33, .39]	**β = .39** 95% CI [.11, .67]**	β = .15 95% CI [−.20, .49]	β = −.06 95% CI [−.42, .30]
Response-locked	−100–000	Weak	β = .09 95% CI [−.24, .42]	β = .22 95% CI [−.08, .52]	β = .33† 95% CI [−.01, .67]	β = −.04 95% CI [−.41, .34]
		Strong	β = .01 95% CI [−.33, .35]	β = .05 95% CI [−.24, .34]	**β = .38* 95% CI [.05, .70]**	β = .01 95% CI [−.30, .32]

Note. Multiple regression analyses were limited to overall RT (i.e., collapsed across conditions) and the most theoretically relevant time windows with either between- or within-group differences (i.e., shaded region Figure 2A and shaded region Figure 3D). LRP amplitudes reflect time windows in which there was a negative deflection associated with the correct response. Models reflect multiple regression analyses controlling for baseline symptoms or functioning for the corresponding outcome variable. Significant findings are bolded. β = standardized β; RT = reaction time; LRP = lateralized readiness potential; GFS:S = Global Functioning Scale: Social; GFS:R = Global Functioning Scale: Role; CI = confidence interval. *df* = (2, 30) for symptoms and (2, 26) for social and role functioning.
† $p = .06$. * $p < .05$. ** $p < .01$.

positive symptoms (β = .02, $p = .91$), social functioning (β = −.21, $p = .21$), or role functioning (β = −.03, $p = .89$).

ERP Measures

There was a Group × Condition interaction in the 200 to 300 ms time window for the stimulus-locked waveforms (Figure 2A shaded region) driven by a between-group difference in the weak response competition condition. In addition, there was a Group × Condition interaction in the −100 to 0 ms time window for the response-locked waveforms (Figure 3D shaded region) driven by a within-group difference in the CHR group. Thus, we focus on relationships between ERP measures within these time windows and baseline and 12-month follow-up symptoms and functioning.

200–300 ms Stimulus-Locked Time Window. Regarding the 200 to 300 ms time window for the stimulus-locked waveforms, smaller (less negative) LRP amplitude associated with activation of the correct response in the weak response competition condition (shaded region Figure 2A) was significantly associated with worsening of negative symptoms at 12-month follow-up (β = .39, $p = .007$).

−100 to 0 ms Response-Locked Time Windows. Regarding associations between ERP measures in the response-locked waveforms within the −100 to 0 ms time window (shaded Region Figure 3D), smaller (less negative) LRP amplitude in the strong response competition condition was counterintuitively significantly associated with improvement of social functioning at 12-month follow-up (β = .38, $p = .023$). There was also a marginally significant trend toward the same association for the LRP amplitude in the weak response competition condition (β = .33, $p = .06$). However, examination of the scatterplots suggests that these are likely spurious associations driven by a restricted range of the outcome variable and a single outlier. With removal of the outlier, these associations were no longer significant (strong-response competition: β = .27, $p = .10$; weak response competition condition: β = .13, $p = .45$).

Discussion

To our knowledge, this was the first study to examine impairments in motor activation and preparation as potential mechanisms of motor dysfunction in individuals at clinical high-risk for psychosis. Specifically, the present study sought to determine if individuals that meet CHR criteria exhibited similar reductions in LRP amplitude as those observed in patients with schizophrenia, and further, if this reduction was attributable to difficulties with overcoming competition from the incorrect response (i.e., a cognitive control deficit) or reflects a more basic motor impairment in activating and preparing responses more broadly.

Overall, our behavioral and neural results were consistent with a basic motor activation deficit in CHR. Specifically, we found that CHR participants exhibited overall slower RTs compared with healthy controls, which is consistent with work in schizophrenia using flankers paradigms demonstrating overall slower responding in patients compared with controls irrespective of response competition (Ettinger et al., 2018; Foti et al., 2012; Kappenman et al., 2012; Mathalon et al., 2002). Similarly, the extent of slowing in the CHR group (i.e., approximately 17 ms) is consistent with the broader CHR literature indicating that those at CHR for psychosis typically exhibit deficits to a lesser degree than patients with formal psychosis (i.e., approximately 60–100 ms; Ettinger et al., 2018; Foti et al., 2012; Kappenman et al., 2012; Mathalon et al., 2002). Regarding neural findings, those that met CHR criteria showed a significant reduction in stimulus-locked LRP amplitude compared with healthy controls under conditions of weak response competition and a significant within group reduction in response-locked LRP amplitude under conditions of weak response competition relative to strong response competition. This is opposite to what would be expected if there was a deficit in cognitive control, which would cause greater impairment under conditions of strong response competition. Indeed, the consistent finding we observed in the strong response competition condition was that the Gratton dip, which directly reflects activation of the incorrect response, did not statistically differ between groups. Again, this is contrary to what would be predicted by a deficit in cognitive control, in which difficulty in exerting cognitive control to inhibit activation of the incorrect response would lead to increased Gratton dip amplitude (Kappenman et al., 2012). Further, consistent with research in both schizophrenia and CHR work (Bernard et al., 2014; Cuesta et al., 2018; Dean et al., 2015; Walther & Strik, 2012), deficits in

motor activation and preparation were associated with worsening of negative symptoms over a 12-month follow-up period.

Overall, these findings are broadly consistent with previous LRP studies in patients with schizophrenia (Hughes et al., 2012; Kang et al., 2019; Kappenman et al., 2012, 2016; Karayanidis et al., 2006; Kieffaber et al., 2007; Luck et al., 2009; Mathalon et al., 2002; Van Voorhis et al., 2019) and implicate basic motor activation and preparation deficits as mechanisms of motor dysfunction in the high-risk period. For example, the present findings are highly consistent with those observed in a study by Kappenman et al. (2012) using a similar flankers paradigm to examine motor activation deficits in patients with schizophrenia. Specifically, Kappenman et al. (2012) found that patients with schizophrenia exhibited reduced LRP amplitude compared with healthy controls with no evidence for increased Gratton dip amplitude under strong response competition contributing to LRP amplitude reductions. In addition, although stimulus-locked waveforms were not examined, Mathalon et al. (2002) also found LRP amplitude reductions and smaller Gratton dip amplitude in patients relative to controls (demonstrating less activation of the incorrect response).

Interestingly, whereas we observed that the amplitude of the Gratton dip was similar for the CHR and HC participants, the subsequent LRP was not blunted in CHR participants compared with controls in the strong response competition condition. Although this finding might be surprising, similar results have been obtained in studies with schizophrenia. For example, Mathalon et al. (2002) found LRP amplitude reductions under conditions of weak response competition in patients, whereas LRP amplitude was comparable between patients and healthy controls under conditions of strong response competition. A similar pattern of results was also observed in Kappenman et al. (2012), such that the LRP reduction in patients was most prominent under conditions of weak response competition. Although more research is needed to understand why the LRP is not as impacted under strong response competition, a comparison between the stimulus- and response-locked waveform findings provide a possible speculation. Specifically, the CHR group exhibited smaller LRP amplitude than controls under conditions of weak response competition in the stimulus-locked, but not response-locked waveforms. Further, healthy controls exhibited a similar LRP amplitude in both the weak and strong response competition conditions in the response-locked waveforms, whereas the CHR participants had a larger LRP when the response competition was strong compared with weak. In other words, the difference between CHR and controls seemed to be driven by a change in LRP amplitude between conditions in the CHR participants. Notably, between-groups differences in stimulus- but not response-locked waveforms is consistent with research in psychosis (Kappenman et al., 2012; Karayanidis et al., 2006; Kieffaber et al., 2007; Luck et al., 2009; Mathalon et al., 2002), and there are several possibilities that may account for these findings.

For example, one possibility is that the incorrect response is actually inhibited (suppressed) under strong response competition, when it is most likely to interfere with selecting the correct response. However, another possibility is that participants may set a higher threshold for how much response activation is needed to execute a response under strong response competition, leading to greater overall activation of the correct response on incompatible trials. Either of these potential explanations would suggest that whereas CHR participants exhibit deficits in motor activation in some instances (i.e., under weak response competition), under conditions where prefrontal control areas are engaged (e.g., under conditions of strong response competition), these cognitive control regions may help compensate for these motor activation deficits. Indeed, there is robust evidence to suggest that higher levels of response conflict signal a stronger need for increased control over action selection (Cavanagh & Frank, 2014; Cavanagh et al., 2009). Further, the direction of the effect for the between-groups differences in the response-locked waveforms (i.e., smaller LRP under conditions of weak response in the CHR group relative to controls), although not significant, was consistent with the between group findings in the stimulus-locked waveforms. Thus, it is also possible that motor processes involved in selecting and preparing motor responses are more affected in the CHR period than motor execution processes. This conclusion is consistent with studies of psychomotor dysfunction in schizophrenia (Osborne, Walther, et al., 2020). Indeed, LRP studies using stop signal paradigms suggest that response selection and preparation processes may be particularly affected (Hughes et al., 2012; Van Voorhis et al., 2019). However, because stimulus- and response-locked waveforms are different means for examining the same LRP component, they inherently reflect a combination of response selection, preparation, and execution processes to varying degrees and these processes cannot be cleanly and completely disentangle within the current study. Thus, it will be important for future studies to determine potential distinct deficits across these response-related processes. Together, these different possible interpretations provide a strong framework for future research using the ERP technique to examine deficits in motor-related processes in the high-risk period and it will be important for future research to investigate these potential hypotheses. Indeed, there are already several studies in patients with schizophrenia to draw from to examine these exact questions (Hughes et al., 2012; Kappenman et al., 2016; Kieffaber et al., 2007; Luck et al., 2009; Van Voorhis et al., 2019).

It is important to note that, although the aforementioned and present findings indicate that LRP reductions across the psychosis spectrum largely reflect primary motor deficits rather than impairments in cognitive control, cognitive control deficits are well-established in the psychosis literature (Lesh et al., 2011) and may still contribute to or exacerbate motor impairments in some situations. For instance, a recent study found that healthy controls exhibited an earlier and larger LRP under speeded compared with unspeeded task instructions, whereas patients with schizophrenia showed no change in the LRP based on task demands, implicating a deficit in top-down control over motor responses (Kappenman et al., 2016). Further, evidence from stop signal paradigms implicate reactive response inhibition, which requires cognitive control to inhibit an already initiated response, in psychosis (Van Voorhis et al., 2019). Notably, these manipulations of cognitive control are quite different than the one used in the current study, and therefore may reflect different aspects of cognitive control than the processes required in the presence of response competition. Thus, future work will be needed to determine whether and to what extent motor processes are affected by top-down deficits in cognition in the high-risk period.

The pathophysiological implications for the current findings may be best understood within a dual-process model of response competition (see Ridderinkhof et al., 2021). In contrast to

traditional informational processing models wherein it is assumed that each stage of processing (e.g., decision making, response) is discrete and performed serially, dual-process models argue that the brain simultaneously engages automatic motor activation and preparation processes while also engaging in top-down decision making (Cisek & Kalaska, 2010; Ridderinkhof et al., 2021). This dual processing of motor and cognitive processes results in adaptive and efficient actions because motor programs are already activated and ready to execute once a response is selected. However, under conditions of strong response competition (i.e., incongruent flankers), response conflict occurs when the incorrect response is initially activated due to the predominate incongruent flankers and the correct decision is selected regarding the direction of the central target (Ridderinkhof et al., 2021). Evidence from nonhuman primate and neuroimaging research suggests that the neural structures implicated in prominent pathophysiological models of psychosis overlap heavily with the fronto-parietal and dopamine-mediated fronto-striatal regions that govern the cognitive control processes required for overcoming response conflict, and the fronto-striatal-thalamic loops involved in activating and preparing responses (Andreasen et al., 1998; Andreasen & Pierson, 2008; Howes & Kapur, 2009; Osborne, Walther, et al., 2020). Thus, the current findings are consistent with the notion that there are likely distinct deficits within fronto-striatal-thalamic loops that contribute to motor activation and preparation impairments in the high-risk period that are consistent with what is observed in formal psychosis, and that these deficits may be largely independent of abnormalities within fronto-parietal regions. Taken together, the present findings provide electrophysiological evidence that impairments in basic motor processing are likely not solely consequences of the disorder or illness-related confounds, and instead may be part of its core pathophysiology.

Indeed, the relationships between ERP measures and baseline and worsening of symptoms observed in the current study further illustrate that motor dysfunction is an important area of research for understanding the pathophysiology of psychosis. Critically, consistent with longitudinal findings from behavioral and clinician rated motor abnormalities in those at CHR for psychosis demonstrating relationships between motor deficits and progression of negative but not positive symptoms (Bernard et al., 2014; Dean & Mittal, 2015; Dean et al., 2014, 2015; Mittal et al., 2014), smaller (less negative) LRP amplitude in the weak response competition condition predicted worsening of negative but not positive symptoms over a 12-month follow-up period. This finding extends the field's understanding of the pathophysiology of psychosis by providing the first electrophysiology evidence for a potential distinct neural mechanism of motor dysfunction being associated with symptom progression in the high-risk period.

A strength of the current study is its ability to rule out any potential effects of antipsychotic medication on the motor activation and preparation deficits observed in the CHR group. Further, the current study design and findings afforded convincing evidence that overcoming response competition does not substantially contribute to motor deficits in activating behavioral responses in the high-risk period. There were also several limitations to the current study. For example, owing to the relatively small sample size and low cumulative risk for conversion over a 12-month period (Salazar de Pablo et al., 2021), no CHR participants converted to formal psychosis over the 12-month follow-up period, precluding the examination of potential associations between deficits in motor activation and conversion. However, the current findings provide novel associations between electrophysiology indices of motor activation and worsening of symptoms and functioning and speak to the potential importance of including measures of motor activation in large-scale consortium studies, as there are currently very few vulnerability markers for negative symptom progression in the high-risk period. Further, although the current task paradigm allowed us to examine the influence of response competition on LRP amplitude, the presence of the Gratton dip made it difficult to characterize LRP latency because of the overlap between the components (Luck, 2014). Specifically, it would be difficult to unambiguously determine if potential shifts in latency were due to latency changes in the Gratton dip or the following negative deflection LRP. This limitation resulted in not being able to directly examine potential slowing of response selection and execution processes. Given that there is evidence for delays in LRP onset latency in patients with schizophrenia (Kappenman et al., 2012, 2016; Karayanidis et al., 2006; Luck et al., 2009), it will be an important area of future research in CHR studies to determine whether similar delays are present before illness onset. Lastly, owing to time constraints and in an effort to limit participant burden, we were not able to include a battery of motor measures; thus, it will be important for future work to validate and extend the current findings by examining potential associations between ERP measures and behavioral and clinician-rated motor abnormalities.

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