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Authors

Oestreich, Lena KL
Mifsud, Nathan G
Ford, Judith M
et al.

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Subnormal Sensory Attenuation to Self-Generated Speech in Schizotypy: Electrophysiological Evidence for a 'Continuum of Psychosis'

Lena K. L. Oestreich[a], **Nathan G. Mifsud**[a], **Judith M. Ford**[b], **Brian J. Roach**[b], **Daniel H. Mathalon**[b], and **Thomas J. Whitford**[a,*]

[a]School of Psychology, UNSW Australia, Sydney, NSW, Australia

[b]Brain Imaging and EEG Laboratory (BIEEGL), Department of Psychiatry, University of California - San Francisco, San Francisco, CA, USA

Abstract

Background—A 'continuum of psychosis' refers to the concept that psychotic-like experiences occur to certain extents in the healthy population and to more severe extents in individuals with psychotic disorders. If this concept is valid, neurophysiological abnormalities exhibited by patients with schizophrenia should also be present, to an attenuated degree, in non-clinical individuals who score highly on the personality dimension of schizotypy. Patients with schizophrenia have consistently been shown to exhibit electrophysiological suppression abnormalities to self-generated speech. The present study aimed to investigate whether these electrophysiological suppression abnormalities were also present in non-clinical individuals who scored highly on schizotypy.

Methods—Thirty-seven non-clinical individuals scoring High (above median) and 37 individuals scoring Low (below median) on the Schizotypal Personality Questionnaire (SPQ; a commonly used schizotypy scale) underwent electroencephalographic (EEG) recording. The amplitude of the N1 component of the auditory-evoked potential was measured while participants (a) vocalized simple syllables (Talk condition), (b) passively listened to a recording of these vocalizations (Listen condition) and (c) listened to a recording of the vocalizations whilst simultaneously watching a video depicting the sound-wave of the forthcoming vocalizations, allowing them to be temporally predicted (Cued Listen condition).

Results—The Low Schizotypy group exhibited significantly reduced N1-amplitude in the Talk condition relative to both the Listen and Cued Listen conditions; that is, they exhibited significant N1-suppression. The High Schizotypy group exhibited significantly lower levels of N1-

*Corresponding author: Dr. Thomas J. Whitford, School of Psychology, UNSW Australia, Sydney, NSW, 2052, Australia, Phone: +61293853936, t.whitford@unsw.edu.au.

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suppression compared to the Low Schizotypy group. Furthermore, whilst the Cued Listen condition induced significantly lower N1-amplitudes compared to the Listen condition in the Low Schizotypy group, this was not the case for the High Schizotypy group.

Conclusions—The results suggest that non-clinical, highly schizotypal individuals exhibit subnormal levels of N1-suppression to self-generated speech, similar to the N1-suppression abnormalities which have previously been reported in patients with schizophrenia. This finding provides empirical support for the existence of a neurophysiological 'continuum of psychosis'.

Keywords

Electroencephalography (EEG); sensory suppression; schizophrenia; schizotypy; continuum of psychosis; self-monitoring; event-related potential (ERP)

1. Introduction

The concept of schizotypy describes various psychosis-like experiences that occur in non-clinical individuals of the general population (Rado, 1953). The quantity and severity of these experiences fall below the level that would qualify them as clinically significant, and these experiences generally do not impair daily functioning (Meehl, 1962). Yet there is evidence to indicate that individuals who score highly on scales of schizotypy have an underlying vulnerability to develop psychotic disorders such as schizophrenia (Lenzenweger, 2010). Advantages of studying schizotypy are that the clinical and demographic confounds typically associated with studying schizophrenia, such as medication, comorbidities and downward social mobility can be avoided (Lenzenweger, 2010).

The concept of schizotypy is closely tied in with a proposed 'continuum of psychosis' (Van Os et al., 2009), whereby psychotic-like experiences exist on a continuum throughout the population. According to this model, non-clinical individuals are prone to experience low-to-intermediate levels of psychotic-like symptoms, while individuals diagnosed with schizotypal personality disorder (SPD) experience higher levels and individuals diagnosed with an established psychotic disorder, such as schizophrenia, experience very high levels of these symptoms (Krabbendam et al., 2004). While schizotypy describes a latent collocation of personality traits typically associated with schizophrenia and SPD, it should be emphasized that high levels of schizotypy are not diagnostic of schizophrenia, and that non-clinical, highly schizotypal individuals typically do not exhibit overt psychotic symptoms and behaviors (Claridge, 1996). Furthermore, the concept of schizotypy does not imply that healthy individuals who score highly on measures of schizotypy are necessarily more 'ill' than individuals who score lower. On the contrary, some aspects of schizotypy have been linked to creativity and academic achievement and may be regarded as beneficial (Nettle, 2005).

If the concept of a 'continuum of psychosis' is valid, it might be expected that non-clinical individuals who score highly on measures of schizotypy would exhibit neurophysiological characteristics that are comparable (but potentially less marked) than those exhibited by individuals with schizophrenia. Patients with schizophrenia fail to suppress the

electrophysiological consequences of self-generated speech (Ford et al., 2001a; Ford & Mathalon, 2004; Ford et al., 2007a; Ford et al., 2007b). These electrophysiological self-suppression abnormalities are theoretically important, as they provide a direct and plausible explanation for schizophrenia patients' bizarre yet characteristic tendency to misperceive sensations resulting from self-generated actions and thoughts as coming from external agents (Feinberg, 1978; Frith, 1995, Whitford et al., 2012).

The N1 component is the largest negative component of the auditory event-related potential (ERP), which typically occurs 80 to 120ms after the presentation of an auditory stimulus. Evidence from fMRI studies suggests that N1 is generated in the primary auditory cortex (Zouridakis et al., 1998). The amplitude of the N1 component is dependent on stimulus intensity; that is, all else held equal, high intensity sounds evoke larger N1 components than do low intensity sounds (Picton et al., 2000). Numerous previous studies with healthy control participants have shown that the amplitude of the N1 component is significantly reduced (i.e. suppressed) when participants self-initiate auditory sensations compared to when passively listening to a recording of the same sounds. N1-suppression has been reported both to tones self-initiated via a button-press (McCarthy & Donchin, 1976; Schafer & Marcus, 1973; Ford et al., 2014; Martikainen et al., 2005) and to speech initiated by willed vocalizations (Ford et al., 2001a; Ford & Mathalon, 2004; Ford et al., 2007a; 2007b; Curio et al., 2000; Houde et al., 2002). N1-suppression – particularly to willed vocalizations – has been interpreted as being caused by an efference copy/corollary discharge mechanism that predicts and suppresses the sensory consequences of self-generated actions. Recordings of neuronal activity in the temporal cortex during neurosurgery found that neuronal firing was suppressed during overt speech compared to passive listening (Creutzfeldt et al., 1989), and this suppression appeared to be highly localized to circumscribed areas within the auditory cortex (Chen et al., 2011; Greenlee et al., 2011).

A substantial body of evidence has accumulated indicating that patients with schizophrenia exhibit reduced levels of N1-suppression to self-generated vocalizations, relative to healthy controls (Ford et al., 2001a; Ford & Mathalon, 2004; Ford et al., 2007a; 2007b). This suggests that at a basic neurophysiological level, schizophrenia patients fail to distinguish between self-generated and externally-generated vocalizations, possibly as a result of abnormalities in underlying corollary discharge mechanisms.

The current paper has two primary aims. First, if the concept of a 'continuum of psychosis' is valid and deficient N1-suppression represents a neurophysiological marker of psychotic-like experiences, then highly schizotypal but non-clinical individuals would be expected to exhibit subnormal levels of N1-suppression relative to low schizotypy individuals. However, to date, N1-suppression during willed vocalization has not been investigated in the context of schizotypy. The present study tested this hypothesis by comparing a sample of healthy, highly schizotypal individuals (defined on the basis of their score on the Schizotypal Personality Questionnaire (SPQ; Raine, 1991)) to a sample of low schizotypy individuals on a modified version of the talk/listen paradigm originally developed by Ford et al. (2001b).

Second, the majority of previous studies on N1-suppression have compared the amplitude of the N1 component evoked by self-generated vocalizations in an active 'talking' condition

with the amplitude of N1 evoked by passively 'listening' to a recording of the vocalizations generated in the 'talking' condition. However, as previously noted, while the auditory stimulus is physically identical in both conditions, there is nonetheless a substantial difference between the conditions in that vocalizations are temporally predictable in the 'talking' condition, as speakers vocalize whenever they choose, a confound noted by Hughes et al. (2013). This raises the possibility that N1-suppression is due, at least in part, to differences in temporal predictability between the conditions, rather than true sensory suppression resulting from corollary discharge mechanisms *per se*. The present study explored this issue by adding a third experimental condition, dubbed the 'Cued Listen' condition, to the 'Talk' and 'Listen' conditions that are typically used in experiments of this nature. In the 'Cued Listen' condition, participants passively listened to a recording of their willed vocalizations (as per the 'Listen' condition) but were cued as to the imminent onset of each vocalization by watching a video of their vocalization waveform. The 'Cued Listen' condition represents a superior comparison condition than the typical 'Listen' condition, given that the cued vocalizations are externally-generated (as per the 'Listen' condition) yet temporally predictable (as per the 'Talk' condition).

Based on the aforementioned findings in patients with schizophrenia, it was hypothesized that participants scoring high on schizotypy would show less N1-suppression in the Talk condition compared to both the Listen and the Cued Listen conditions, compared to low schizotypy participants. In contrast, low schizotypy participants were expected to show significant N1-suppression in the Talk condition relative to both Listen and Cued Listen, reflecting the operation of a corollary discharge mechanism to self-generated speech. Furthermore, we also predicted that the low schizotypy participants would show significantly reduced N1-amplitudes in the Cued Listen condition relative to the Listen condition, reflecting the effects of temporal predictability.

2. Material and methods

2.1 Participants

Seventy-five participants were recruited through online recruitment systems (SONA-1 and SONA-P) at UNSW, Australia. Participants from the SONA-1 recruitment system were first-year psychology student who were reimbursed for their time with course credit. SONA-P is an online recruitment system, which is open for everyone to enrol and offers participants financial reimbursement for their time. Participants' demographic data, alcohol, nicotine and caffeine consumption, recreational drug use, exclusion criteria and scores on the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) are displayed in Table 1. Estimates of drug use and history of Axis 1 disorders were also based on participants' self-report. One participant was excluded due to a self-reported diagnosis of an Axis I disorder, based on DSM-IV-TR criteria (American Psychiatric Association, 2000). Participants were assigned to Low (n=37) and High (n=37) Schizotypy groups based on a median split of their score on the SPQ. (In a supplementary analysis, described in the Supplementary Materials section, participants were divided into more extreme schizotypy groups, where participants scoring in the upper quartile were assigned to the High Schizotypy group (n=21) and participants scoring in the lower quartile to the Low Schizotypy group (n=21)). The

schizotypy groups did not differ in self-reported consumption of caffeine, alcohol, nicotine or recreational drugs. Fifty-nine percent of participants reported that English was not their native language. However, there was no significant difference between the groups on this measure, and all individuals were able to converse fluently in English, which is an admission requirement by UNSW, Australia. After explaining the procedure of the study and providing an opportunity to participants to ask questions for clarification, all participants gave written informed consent. This study was approved by the UNSW Human Research Ethics Advisory Panel (Psychology).

2.2 Procedure

The first part of the experiment included a battery of questionnaires and self-report measures. The questions asked about participants' demographic information, whether their first language was English, as well as alcohol, nicotine and caffeine consumption. Estimates of drug use and history of Axis 1 disorders were also based on self-reports. Following these questionnaires, participants completed the SPQ. Participants then underwent an electroencephalography (EEG) recording session during which they were seated in a quiet, dimly-lit room, one meter in front of a computer monitor (BenQ XL2420T, 144Hz, 24″W, 3D-ready LED).

There were three conditions in the EEG experiment: Talk, Listen and Cued Listen. The protocol for the Talk and Listen conditions were based on the previously published protocol by Ford et al. (2010), while the protocol for the Cued Listen condition was a refinement of the protocol used by Ford et al. (2007a). In the Talk condition, an instruction video was first played in which participants were instructed how to vocalize the syllable 'ah' in a clear and sharp manner while maintaining their gaze on a fixation cross. In a practice task, participants were trained to vocalize the syllable 'ah' with intensity between 75dB and 85dB and duration of less than 300ms. In the main task, participants were instructed to vocalize a series of 'ah's, every one to three seconds for three minutes while maintaining their gaze on a fixation cross. Participants vocalized into a desk-mounted microphone (Keenion MIC-309, frequency response: 100–16,000Hz, impedance: 2,000Ω, sensitivity: −48dB,), producing between 75 and 125 'ahs' in this three minute period (M = 110.89, SD = 23.92). The output from the microphone was split into two output channels. The first output channel was sent directly to participants' headphones (Shintaro, frequency response: 100–15,000Hz, impedance: 32Ω, sensitivity: 101dB 4dB, maximum power input: 100mW) such that participants heard their own vocalizations in their headphones, in real time. The second output channel was sent to a second set of speakers (Philips SHL 3000/00, frequency response: 20–20,000 Hz, impedance: 24Ω, sensitivity: 106dB, maximum power input: 1000mW) from which a microphone (Shure SM58, frequency response: 50–50,000Hz, impedance: EIA rated at 150Ω (300Ω, actual), sensitivity: −54.5dBV/Pa (1.85mV)) connected to the EEG amplifier was continuously recording; this enabled the recording of a 'sound' channel in the EEG that was synchronized with the sounds that participants were actually hearing. Each participant's three-minute time series of utterances was recorded with the audio manipulation software Audacity (2012).

In the Listen condition, participants were instructed to relax, sit silently and focus on the fixation cross while the three-minute time-series of their willed vocalizations, recorded during the Talk condition, was played back through their headphones. The Cued Listen condition was identical to the Listen condition except that participants were instructed to watch a video depicting a sound wave of their vocalization time-series while they listened to the audio of their recorded vocalizations. As illustrated in Figure 1, a line that was synchronized with the audio of the vocalizations moved across the sound-wave such that participants could predict exactly when they were going to hear each 'ah' in the time-series.

2.3 Data Acquisition and Analysis

EEG data were acquired with a BioSemi ActiView system (Biosemi, Netherlands) with the following specifications: 2048Hz sample rate, 417Hz bandwidth (3db), 18 dB/octave roll-off. An electrode cap was used with Ag/Ag-Cl electrodes from 64 sites referenced to internal sensors located in the parietal lobe of the cap. During pre-processing, data were referenced off line to the average of the mastoid electrodes. Further electrodes were placed on the outer canthi of both eyes and below the left eye to measure eye blinking and movement (vertical and horizontal electrooculogram; VEOG, HEOG). Triggers were inserted in the EEG data at the onset of each 'ah', which was defined using the 'Level Trigger' function on the microphone channel in BrainVision Analyzer. EEG data were segmented into 800ms intervals, consisting of 200ms before and 600ms after the onset of each 'ah'. A regression based algorithm was adopted to correct for eye blinks and movements in the EEG using VEOG and HEOG based on the protocol of Gratton et al. (1983). Low and high frequencies were attenuated using a 0.5 – 15Hz bandpass filter (Ford & Mathalon, 2004). Trials containing motor artifacts, which were defined as voltages exceeding ± 50μV, were rejected. The remaining artifact free trials in the Talk, Listen and Cued Listen conditions were averaged to event-related potential (ERPs) for each participant respectively. The N1 component of each ERP was identified as the most negative peak between 50ms and 150ms after speech onset. ERPs were baseline corrected using the 100ms interval preceding the speech sounds. The electrode Cz was investigated because of the characteristically large amplitude of the N1 component elicited by bilateral auditory stimulation at this site (Luck, 2005).

2.4 Statistical Analysis

Statistical analysis was performed using SPSS (IBM Corp., 2012). In order to examine the effect of condition on N1 amplitude at electrode Cz, a 2*(3) mixed Analysis of Variance (ANOVA) was conducted. The between-subjects factor was *group* (High Schizotypy/Low Schizotypy) and the within-subjects factor was *condition* (Talk/Listen/Cued Listen). In the case of a significant main effect or interaction, supplementary 2*(2) mixed ANOVAs were employed to identify the cause of the omnibus effect. Where main effects or interactions were found to be significant, follow-up contrasts (Fisher's Least Significant Difference) were used to investigate the underlying simple effects.

3. Results

3.1 High vs Low Schizotypy (Median Split)

The mean score on the SPQ of the entire participant sample was 22.38 (*SD* = 15.54, Range = 1–57), and the median was 19.50. A median split was used to define the 37 participants who scored below 20 on the SPQ (*M* = 10.05, *SD* = 5.41) as the Low Schizotypy group while the 37 participants who scored equal or higher than 20 on the SPQ (*M* = 34.70, *SD* = 12.18) constituted the High Schizotypy group (see Table 1).

Independent samples t-tests revealed that there were significant differences between the High and Low Schizotypy groups on age and handedness (see Table 1). To control for these between-group differences, these two variables were centered and covaried for in the statistical analysis.

An omnibus mixed ANCOVA revealed a significant main effect of *condition* (Talk/Listen/Cued Listen) on N1 amplitude at electrode Cz [$F(2,140) = 20.664$, $p < 0.001$, $\eta_p^2 = 0.228$]. There was no significant main effect of *group* (High Schizotypy/Low Schizotypy) [$F(1,70) = 0.996$, $p = 0.322$, $\eta_p^2 = 0.014$]. There was, however, a significant *group*condition* interaction [$F(2,140) = 5.239$, $p = 0.021$, $\eta_p^2 = 0.070$] (see Fig. 2 and Fig. 3).

A complementary 2*(2) ANOVA comparing N1-amplitude in the Talk and Listen conditions revealed a significant main effect of *condition* (Talk/Listen) [$F(1,70) = 25.566$, $p < 0.001$, $\eta_p^2 = 0.268$]. There was no significant main effect of *group* (High Schizotypy/Low Schizotypy) [$F(1,70) = 1.589$, $p = 0.212$, $\eta_p^2 = 0.022$]. There was, however, a significant *group*condition* interaction [$F(1,70) = 6.371$, $p = 0.014$, $\eta_p^2 = 0.083$]. Follow-up analysis of the Talk/Listen comparison revealed that while the High Schizotypy group exhibited only a trend reduction in N1-amplitude in the Talk condition relative to the Listen condition [$t(36) = 1.667$, $p = 0.100$, Cohen's $d = 0.458$], the Low Schizotypy group exhibited a significant reduction in N1-amplitude in the Talk condition relative to the Listen condition [$t(36) = 5.325$, $p < 0.001$, Cohen's $d = 1.137$] (see Fig. 2 and Fig. 3).

A complementary 2*(2) ANOVA comparing N1-amplitude in the Talk and Cued Listen conditions revealed a significant main effect of *condition* (Talk/Cued Listen) [$F(1,70) = 15.314$, $p < 0.001$, $\eta_p^2 = 0.180$]. There was no significant main effect of *group* (High Schizotypy/Low Schizotypy) [$F(1,70) = 3.251$, $p = 0.076$, $\eta_p^2 = 0.044$]. There was, however, a significant *group*condition* interaction [$F(1,70) = 4.108$, $p = 0.046$, $\eta_p^2 = 0.055$]. Follow-up analysis of the Talk/Cued Listen comparison revealed that the High Schizotypy group did not show a significant reduction in N1-amplitude in the Talk condition relative to the Cued Listen condition [$t(36) = 1.238$, $p = 0.220$, Cohen's $d = 0.349$]. In contrast, the Low Schizotypy group did show a significantly reduced N1 amplitude in the Talk condition compared to the Cued Listen condition [$t(36) = 4.174$, $p < 0.001$, Cohen's $d = 0.849$].

A complementary 2*(2) ANOVA comparing N1-amplitude in the Listen and Cued Listen conditions revealed a significant main effect of *condition* (Listen/Cued Listen) [$F(1,70) = 20.522$, $p < 0.001$, $\eta_p^2 = 0.227$]. There was no significant main effect of *group* (High

Schizotypy/Low Schizotypy) [$F(1,70) = 0.452$, $p = 0.504$, $\eta_p^2 = 0.006$]. There was, however, a significant *group*condition* interaction [$F(1,70) = 4.080$, $p = 0.047$, $\eta_p^2 = 0.055$]. Follow-up analysis of the Cued Listen/Listen comparison revealed that while the High Schizotypy group did not show significantly reduced N1-amplitude in the Cued Listen condition relative to the Listen condition [$t(36) = 1.665$, $p = 0.10$, Cohen's $d = 0.164$], the Low Schizotypy group did show a significant difference in N1-amplitude between these two conditions [$t(36) = 4.592$, $p < 0.001$, Cohen's $d = 0.515$].

For completeness, in terms of between-group contrasts, N1-amplitude to the Talk condition in the Low Schizotypy group was significantly reduced compared to the Talk condition in the High Schizotypy group [$t(73) = 2.120$, $p = 0.038$, Cohen's $d = 0.491$]. N1-amplitude did not differ significantly between the Low and High Schizotypy groups in either the Listen condition [$t(73) = 1.216$, $p = 0.228$, Cohen's $d = 0.205$] or the Cued Listen condition [$t(73) = 0.010$, $p = 0.922$, Cohen's $d = 0.097$].

3.2 Supplementary Analysis

In order to further investigate the effect of schizotypy on N1-suppression, participants were divided into more extreme groups, where the Low Schizotypy group was comprised of participants scoring in the bottom quartile on the SPQ and the High Schizotypy group was defined as participants scoring in the top quartile (see Supplementary Materials). The results showed the same overall pattern as when the groups were defined by a median split.

All analyses were also repeated with the electrodes Fz and FCz. These analyses yielded the same overall pattern as for the results reported for electrode Cz, and are therefore not presented separately.

3.3 Correlations with the SPQ

N1-suppression between Talk and Listen conditions (i.e., $N1_{Talk - Listen}$) was calculated by subtracting N1 amplitude in the Listen condition from N1 amplitude in the Talk condition. Similarly, N1-suppression between Talk and Cued Listen conditions (i.e., $N1_{Talk - Cued}$) was determined by subtracting the Cued Listen condition from the Talk condition. Participants'SPQ scores were found to be significantly negatively correlated with both $N1_{Talk - Listen}$ [$r = -0.297$, $p = 0.010$] and $N1_{Talk - Cued}$ [$r = -0.260$, $p = 0.025$] – see Figure 4 and 5. These results indicated that as participants' level of N1-suppression increased, their SPQ score decreased. For N1-suppression $N1_{Talk – Listen}$ ($M = 2.808$, $SD = 4.876$) two outliers (> 3*SD* from the mean) were identified. After excluding these outliers, the correlation remained significant [$r = -0.325$, $p = 0.005$]. For N1-suppression $N1_{Talk – Cued}$ ($M = 2.079$, $SD = 4.595$) one outlier was identified. After excluding this outlier, the correlation remained significant [$r = -0.259$, $p = 0.027$].

4. Discussion

The primary aim of the present study was to investigate whether N1-suppression abnormalities that have previously been reported in patients with established schizophrenia in response to self-generated vocalizations (Ford et al., 2001a; Ford & Mathalon, 2004; Ford et al., 2007a; 2007b) were also present in non-clinical individuals who scored high on the

personality dimension of schizotypy. The results of the present study support this contention; that is, while healthy participants who scored below the median on the SPQ exhibited N1-suppression to self-generated vocalizations compared to identical externally generated vocalizations (both cued and uncued), participants who scored above the median did not exhibit N1-suppression to self-generated vocalizations. The same pattern of results was found when comparing participants who scored in the upper and lower quartiles of the SPQ. Finally, participants' total scores on the SPQ were significantly negatively correlated with their level of N1-suppression, such that participants with the highest level of schizotypy exhibited the lowest level of N1-suppression. The results of this study indicate that N1-suppression abnormalities are not specific to patients with schizophrenia, but are instead associated with high levels of schizotypy more generally. By providing evidence that the neurophysiological abnormalities associated with schizophrenia are present, at least to some degree, in healthy individuals with above average levels of schizotypy, this study provides empirical evidence for the concept of a 'continuum of psychosis' (Van Os et al., 2009; Krabbendam et al., 2004).

Several previous studies have observed non-clinical individuals high in schizotypy to show the same behavioral and neurophysiological deficits as found in patients with established schizophrenia, including deficits in sense of agency (Asai & Tanno, 2007; 2008), working memory (Ziermans, 2013; Chun et al., 2013), executive functioning (Kim et al., 2011), attention and prepulse inhibition (Giakoumaki, 2012), as well as resting state fMRI indicating a significant positive correlation between SPQ score and visual resting state networks and a significant negative correlation between SPQ score and auditory resting state networks (Lagioia et al., 2010). However, to our knowledge, the present study is the first to investigate N1-suppression to self-generated speech in the context of schizotypy.

A significant finding in the present study was that when low schizotypy participants were cued as to the imminent arrival of their pre-recorded vocalization (i.e., by watching synchronized video feedback of their own pre-recorded speech), it caused a significant reduction in their N1 response compared to when listening to the same sounds that were not cued. The finding – that cuing participants as to the imminent arrival of a sound reduces the N1-amplitude evoked by that sound – has been reported previously in healthy participants for both willed vocalizations (Ford et al., 2007a) and button-press elicited sounds (McCarthy & Donchin, 1976; Schafer & Marcus, 1973; Ford et al., 2014; Martikainen et al., 2005; Ford et al., 2001b; Whitford et al., 2011; Aliu et al., 2009; Bäss et al., 2011). These results, in combination with the results of the present study, indicate that the temporal predictability of the auditory stimuli affects N1-suppression during talking compared to listening, in so far as predictability affects N1 during the Listen condition. However, it is important to note that the Low Schizotypy group still exhibited N1-suppression in the Talk condition relative to the Cued Listen condition in the present study. That is, N1-suppression was reduced, but not eliminated, when controlling for temporal predictability. This result suggests that N1-suppression of self-generated vocalizations results from a combination of at least two distinct mechanisms: namely (1) the suppressant effects of temporal predictability *per se* (Hughes et al., 2013; Desantis et al., 2012) ('psychological suppression'), and (2) the suppressant effects associated with performing willed motor actions *per se* ('physiological

suppression'), which is a mechanism in which corollary discharges are thought to play a crucial role (Eliades & Wang, 2003; 2008; Hickok, 2012).

While the low schizotypy participants exhibited an attenuated N1-amplitude in the Cued Listen condition, relative to the Listen condition, the high schizotypy participants did not. In other words, cuing the imminent arrival of the vocalizations had no significant effect on N1-amplitude in the high schizotypy participants. This finding was evident regardless of whether the schizotypy groups were defined on the basis of a median split or an extreme-quartile split. In keeping with the proposed distinction between 'psychological' and 'physiological' suppression, it was revealing that high schizotypy participants exhibited reduced suppression compared to low schizotypy participants, in both the Talk minus Cued Listen contrast (which investigated the suppressant effects of performing the vocalization while controlling for temporal predictability) and the Listen minus Cued Listen contrast (which investigated the suppressant effects of temporal predictability *per se*), as it suggests that both 'psychological' and 'physiological' suppression mechanisms were abnormal in the high schizotypy participants. These results are consistent with the study of Ford et al. (2007a), who found that when healthy control participants were warned by means of a visual '3…2…1 style' countdown, about the impending arrival of an auditory stimulus, it resulted in N1 attenuation compared to when the same stimulus was presented in the absence of the warning. Schizophrenia patients, in contrast, did not exhibit this N1-attenuation in response to the visually cued auditory stimuli. Thus, the findings of the present study are important insofar as they imply that highly schizotypal individuals, like schizophrenia patients, possess general deficits in using information to make predictions about imminent future events.

The visual cue used in the present study was an improvement on the cue used by Ford et al. (2007a), as it allowed participants to predict *exactly* when each vocalization was going to occur rather than depending on participants accurately estimating the time between the last cue (1… 'ah') on the basis of the gap between the previous two cues (3…2…1). Furthermore, it is worth noting that in contrast to a '3…2…1' style countdown, participants in the present study were also presumably able to predict the approximate loudness and duration of the impeding speech sound from the size and shape of the sound-wave presented in the video display (see Figure 1). Thus we suggest that a 'video-style' cue such as the one employed in the present study would be a worthwhile addition for future studies aimed at investigating N1-suppression.

Given that one of the main aims of the present study was to investigate the evidence for a neurophysiological continuum of psychosis based on N1-suppression abnormalities, the lack of a clinical schizophrenia group presents a limitation. However, while the majority of studies in patient groups have not included measures of schizotypy such as the SPQ, one study that did (Cadenhead et al. 1999), reported similar scores on the SPQ of patients with schizophrenia (M =30.9, SD = 16.9) and schizotypal personality disorder (M = 34.5, SD = 11.1), to the High Schizotypy group in the present study (M = 35.6, SD = 11.8). Similarly, the Low Schizotypy group of the current study exhibited comparable SPQ scores (M = 10.05, SD = 5.41) to the healthy control group (M = 6.3, SD = 7.9) in the study of Cadenhead et al. (1999). Nevertheless a direct comparison of N1-suppression between patients with schizophrenia and non-clinical participants scoring high and low on schizotypy

would provide further insight into the nature of the hypothesized 'continuum of psychosis', and would therefore represent a fruitful avenue for future research. Finally, it should be emphasized that while the High Schizotypy group exhibited significantly less N1-suppression than did the Low Schizotypy group (as indicated by the significant *group*condition* interaction for Talk/Listen and Talk/Cued Listen), the High Schizotypy group did show some evidence of N1-suppression. The Talk versus Listen contrast in the High Schizotypy group was close to significance ($p = 0.100$), and given that the observed effect size for this contrast was found to be within the low to medium range (Cohen's $d = 0.458$) it is likely that a more powered analysis with a larger sample size would have led to a significant result. Future studies with larger sample sizes are therefore required to clarify this finding.

This study provides empirical evidence for the existence of 'continuum of psychosis' by showing that highly schizotypal, non-clinical individuals exhibit subnormal levels of N1-suppression to self-generated vocalizations, such as have previously been reported in patients with schizophrenia. While a direct comparison between N1-suppression in high schizotypes and N1-suppression in patients with established schizophrenia is lacking at this stage, if the concept of a 'continuum of psychosis' is valid, it would be predicted that highly schizotypal individuals would exhibit N1-suppression levels that were intermediate between low schizotypes and patients with schizophrenia. The results of the present study raise the key question of whether subnormal N1-suppression to self-generated vocalizations could potentially represent a biomarker for schizotypy which could potentially show utility in predicting future transition to psychosis in high-risk individuals. Such a finding would have immense implications as it would open up the possibility of targeting these (neurophysiologically-defined) high-risk participants with prophylactic treatments aimed at preventing transition to florid psychosis (Yung et al., 2007).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- N1-suppression to self-compared to externally generated speech in Low Schizotypes
- High Schizotypes did not exhibit N1-suppression to self-generated vocalizations
- SPQ scores were significantly negatively correlated with level of N1-suppression
- The higher the level of schizotypy, the lower the level of N1-suppression

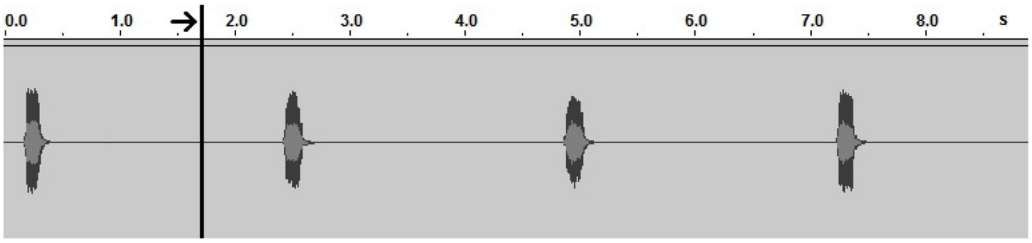

Figure 1.

A graphical representation of the Cued Listen condition. The line, which is synchronized with the audio signal, moves across the spectrograph while participants listen to playback of their willed vocalizations recorded in the Talk condition. This allows participants to predict the onset of each vocalization. Time in seconds.

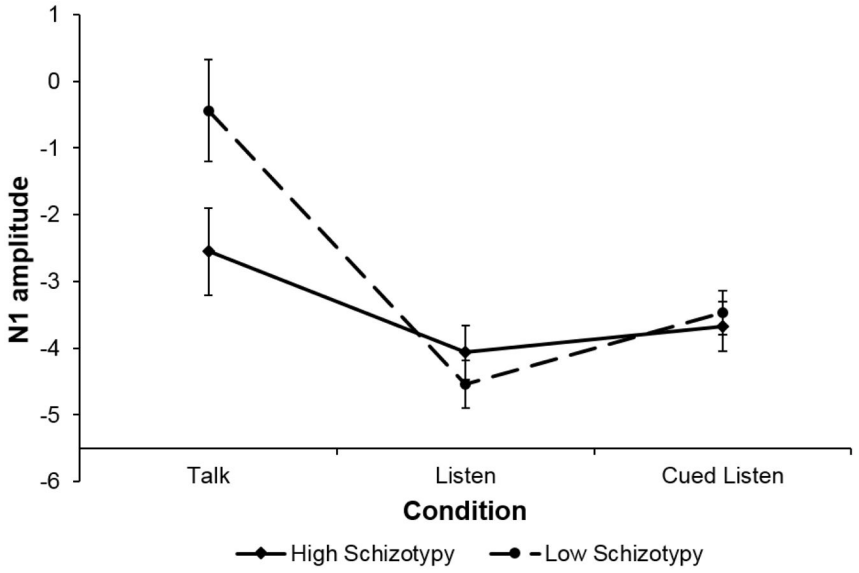

Figure 2.

The relationship between condition (Talk/Listen/Cued Listen) and N1 amplitude (in microvolts) for High and Low Schizotypy groups. Error bars represent standard error of the mean.

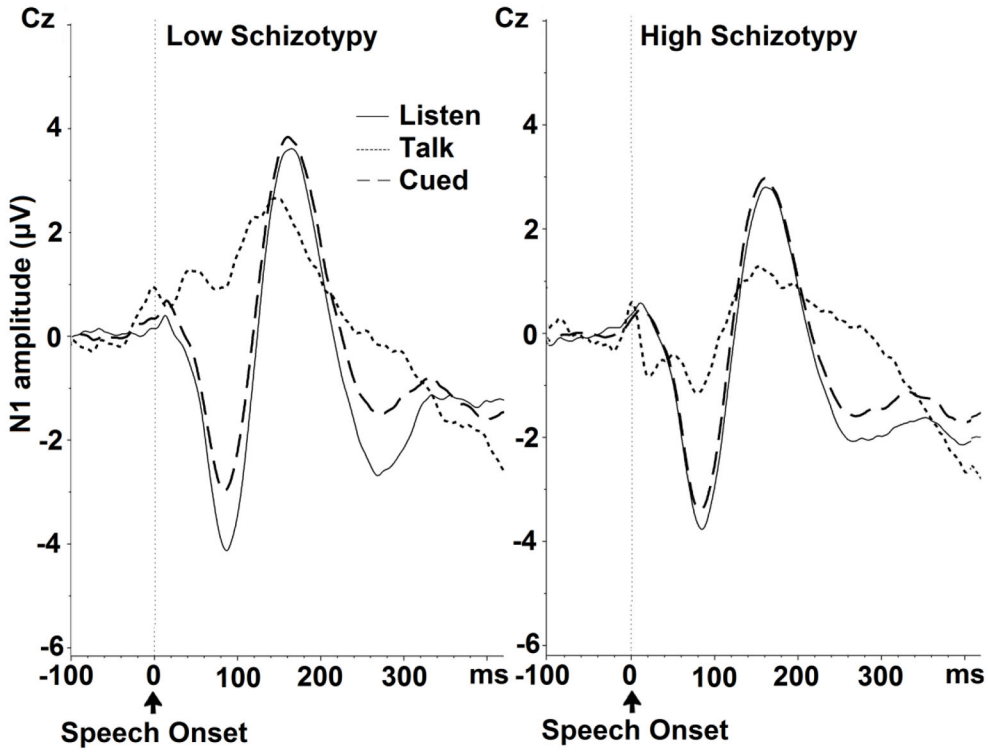

Figure 3.

Event-related potentials (ERPs) from electrode Cz in response to willed vocalizations (‘ah’) in the Listen, Talk and Cued Listen conditions, for the High and Low Schizotypy groups. ERPs are time-locked to the onset of the vocalizations.

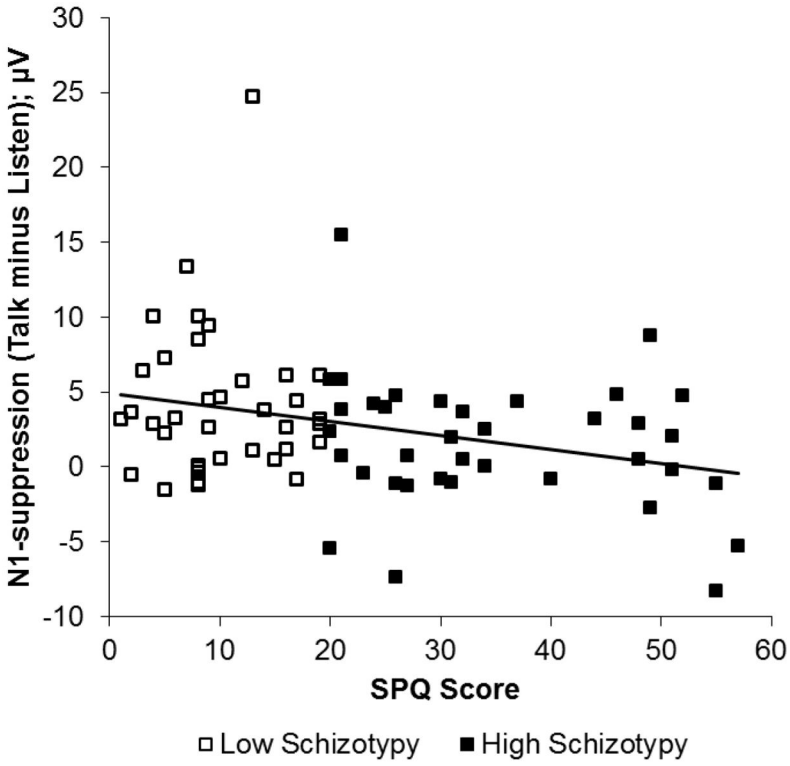

Figure 4.
Correlation between N1-suppression (Talk-Listen) and participants' scores on the Schizotypal Personality Questionnaire (SPQ).

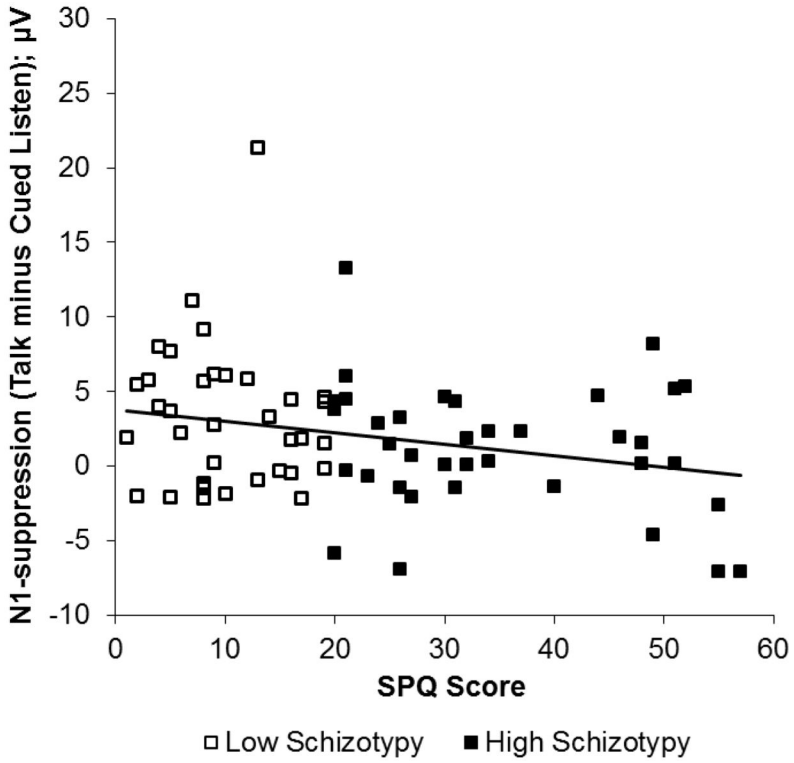

Figure 5.
Correlation between N1-suppression (Talk-Cued Listen) and participants' scores on the Schizotypal Personality Questionnaire (SPQ).

Table 1

Demographics, exclusion criteria and scores on the SPQ

	Low Schizotypy (*n* = 37)			High Schizotypy (*n* = 37)			High vs. Low Schizotypy
Variable	**Mean**	***SD***	**Range**	**Mean**	***SD***	**Range**	
Age (years)	20.57	3.36	18–36	23.24	5.66	18–44	$t(1,59) = 2.47$, $p = 0.016$
Gender (M/F)	12/25			16/22			$\chi^2(1) = 0.919$, $p = 0.338$
First Language (English/non-English)	26/11			18/19			$\chi^2(1) = 3.588$, $p = 0.058$
Household Income[a]	36.3	2.95	1–9	30.8	2.55	1–9	$t(1,55) = -0.73$, $p = 0.466$
Handedness (right/left)	37/0			33/4			$\chi^2(1) = 4.229$, $p = 0.040$
Caffeine[b]	1.12	1.69	0–9	0.75	0.78	0–3	$t(1,72) = -1.21$, $p = 0.229$
Nicotine[c]	0.11	0.66	0–4	0.43	1.02	0–4	$t(1,62) = 1.63$, $p = 0.108$
Alcohol[d]	0.81	1.08	0–4	0.68	1.13	0–6	$t(1,72) = -0.53$, $p = 0.600$
Recreational Drugs[e]	0.19	0.52	0–2	0.30	0.77	0–3	$t(1,72) = 0.70$, $p = 0.484$
Axis I	0/37			1[f]/38			
SPQ total	10.05	5.41	1–19	34.70	12.18	20–57	$t(1,50) = 11.25$, $p < 0.001$
Unusual Perceptual Experiences	0.76	0.98	0–3	2.89	1.88	0–6	$t(1,54) = 6.11$, $p < 0.001$
Suspiciousness	0.95	1.25	0–4	4.19	2.09	0–8	$t(1,59) = 8.10$, $p < 0.001$
Odd Beliefs or Magical Thinking	0.46	0.73	0–3	2.03	1.68	0–5	$t(1,49) = 5.22$, $p < 0.001$
Ideas of Reference	1.24	1.30	0–4	4.62	2.74	0–9	$t(1,51) = 6.77$, $p < 0.001$
Excessive Social Anxiety	1.95	1.91	0–7	5.65	2.30	0–8	$t(1,72) = 7.56$, $p < 0.001$
No Close Friends	0.62	0.76	0–2	3.97	2.51	0–8	$t(1,43) = 7.77$, $p < 0.001$
Constricted Affect	0.89	1.27	0–5	3.22	2.14	0–7	$t(1,58) = 5.70$, $p < 0.001$
Odd or Eccentric Behavior	1.22	1.90	0–6	2.86	2.30	0–7	$t(1,72) = 3.36$, $p = 0.001$
Odd Speech	1.92	1.89	0–6	5.16	2.32	1–9	$t(1,69) = 6.60$, $p < 0.001$

Note. SD = standard deviation; M = male; F = female; SPQ = Schizotypal Personality Questionnaire.

[a] Household income: 1 = *under $10,000*; 2 = *$10,000 – $19,999*; 3 = *$20,000– $29,999*; 4 = *$30,000 $39,999*; 5 = *$40,000 – $49,999*; 6 = *$50,000 – $74,999*; 7 = *$75,000 – $ 99,999*; 8 = *$100,000 – $150,000*; 9 = *over $150,000;* 10 = *Prefer not to say*.

[b] Caffeine: Coffee = *1 unit*, Red Bull = *1.5 units*, Tea, Coca Cola = *0.5 units*.

[c] Nicotine: 0 = *zero*, 1 = *Less than three per week*, 2 = *Less than five per week*, 3 = *A pack a week*, 4 = *More than a pack a week*.

[d] Alcohol: 0 = *zero*, 1 = *1–5*, 2 = *6–10*, 3 = *11–15*, 4 = *16–20*, 5 = *21–25*, 6 = *more than 2*.

[e] Average number of recreational drugs used in past month: 0 = *None*, 1 = *Cannabis*, 2 = *Ecstasy*, 3 = *Amphetamines*, 4 = *Hallucinogens*, 5 = Opiates, 6 = *Prefer not to say*.

[f] Exclusion criterion: self-reported diagnosis with Axis I disorder (DSM-IV-TR).