

Investigation of Emotional Expression Processing Following Cognitive Behavioural Therapy for Patients with Schizophrenia: An Event-Related Potentials Study

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Growing evidence supports the use of cognitive behavioural therapy (CBT) for psychosis, including CBT for voices (CBTv), which targets auditory verbal hallucinations (AVH). The present study observed the effects of CBTv on electrophysiological measures of facial expression processing in patients with schizophrenia with AVH. Twenty-five patients with schizophrenia were randomly assigned to a treatment group (TG; $n = 14$) or a treatment as usual (TAU) group ($n = 11$). The TG received group CBTv for five-six months in addition to their TAU. The matched waitlist group received TAU for the five-six months. The CBTv treatment showed shorter P100 latency in response to facial expressions following treatment compared with baseline, but not the TAU group. Amount of negative content of voices and “omnipotence” of voices were modified following CBTv treatment, but not following TAU. This study provides evidence that CBTv decreases early visual information processing time as indexed by the P100 latency.

Keywords: schizophrenia, cognitive-behavioural therapy, event-related potentials, auditory-verbal hallucinations, face processing

Une quantité grandissante de preuves soutient l'utilisation de la thérapie cognitivo-comportementale (TCC) pour la psychose, dont la TCC pour les voix (TCCv) ciblant les hallucinations auditives verbales (HAV). L'étude relevait les effets de la TCCv sur les mesures électrophysiologiques du traitement de l'expression faciale chez les patients schizophrènes avec HAV. Twenty-five patients étaient affectés aléatoirement au groupe de traitement (GT; $n = 14$) ou du traitement habituel (GTH; $n = 11$). Le GT suivait une TCCv de groupe pendant cinq à six mois en plus du TH. Le groupe apparié en liste d'attente suivait le TH pendant cette période. Uniquement le traitement de TCCv diminuait le temps de latence de P100 par rapport au niveau de base, en réponse aux expressions faciales. La quantité de contenus négatifs et «l'omnipotence» des voix ont changé à la suite de la TCCv seulement. Cette étude supporte que la TCCv diminue le temps de traitement de l'information visuelle.

Mots clés : schizophrénie, thérapie cognitivo-comportementale, potentiels liés aux événements, hallucinations auditives verbales, traitement du visage

Schizophrenia is a psychotic disorder characterized by positive and negative symptoms. Positive symptoms appear to reflect an excess or distortion of normal functions, such as distortions in thought content (delusions) and perception (hallucinations). Negative symptoms reflect the absence of or diminished normal functions, such as disorganized speech, impairment in motivation and

self-monitoring of behaviour (which is observed by grossly disorganized or catatonic behaviour), and deficits in social skills (American Psychiatric Association [APA], 2013).

Persistent positive symptoms such as hallucinations and delusions are severely distressing and disruptive of daily functioning, including social functioning (Kuipers et al., 2006). Auditory hallucinations are a common characteristic of schizophrenia, with prevalence estimates ranging between 40% and 80% (Sommer et al., 2012). Auditory hallucinations are defined as a “sensory perception that has a compelling sense of reality, but which occurs without external stimulation of the sensory organ” (APA, 1994, p.767). Pharmacotherapies are not completely effective in

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treating and reducing distress in patients who experience auditory hallucinations. Many patients remain symptomatic despite adequate doses of antipsychotic drugs (Kane, 1996; Lieberman et al., 2005). The negative impacts of experiencing auditory hallucinations have been found to affect not only the auditory modality, but also extend to impairments in visual processing (Bruder et al., 2011; van Lutterveld, Sommer, & Ford, 2011), including face processing (Kayser et al., 2012). Cognitive Behavioural Therapy (CBT) has been suggested to be a promising approach for improving information processing difficulties in patients with schizophrenia and, by so doing, facilitating social cognition and daily functioning (Pontillo et al., 2016). As such, CBT has been suggested as a complement to pharmacotherapies, specifically to target psychosis in treatment-resistant cases (Pilling et al., 2002a, 2002b; Tarrier & Wykes, 2004; Zimmermann, Favrod, Trieu, & Pomini, 2005).

Patients with schizophrenia usually report high levels of distress in response to auditory hallucinations (Birchwood & Chadwick, 1997; van der Gaag, Hageman, & Birchwood, 2003). Specialized Cognitive Behavioural Therapy for psychosis (CBTp), developed as a psychosocial treatment to decrease patient distress associated with hallucinations and delusions (Haddock et al., 1998), is recommended as an adjunctive treatment for individuals who experience persistent auditory hallucinations (National Collaborating Centre for Mental Health [NCCMH], 2009). Multiple meta-analyses on the effectiveness of CBTp have evaluated treatment effects on the frequency and severity of positive symptoms (Lincoln et al., 2012; Lynch, Laws, & McKenna, 2010; Pfammatter, Junghan, & Brenner, 2006; van der Gaag, Valmaggia, & Smit, 2014; Wykes, Steel, Everitt, & Tarrier, 2008; Zimmermann et al., 2005), negative symptoms (Rector & Beck, 2001), general psychopathology (Sarin, Wallin, & Widerlov, 2011; Wykes et al., 2008), and have found CBTp to result in modest but significant positive impact in controlled studies (average effect around 0.35 - 0.40; Sivec & Montesano, 2012).

CBTp for psychosis is a broad therapy approach allowing patients and clinicians to address any mental health symptom that is problematic for the patient. Several authors have advocated for administering tailored therapy based on specific symptoms, such as hallucinations (Morrison & Barratt, 2010; Steel et al., 2007), rather than administering CBTp that encompasses interventions targeting a broad array of symptoms. Researchers suggest that the effects of CBTp on psychosis symptoms may be greater by using a symptom-specific approach, such as CBT for voices (CBTv; Lincoln & Peters, 2019; van der Gaag et al., 2014), to specifically target auditory hallucinations.

The cognitive model of voice hearing proposes that the distress is related to idiosyncratic beliefs or cognitive appraisals involving factors such as control, power, identity of voice, authority, and consequences of not complying with the voices (Birchwood et al., 2004; Chadwick & Birchwood, 1994; Mawson, Cohen, & Berry, 2010). These beliefs/appraisals impact the individual's emotional, behavioural, and somatic responses to the voice hearing experiences. In turn, emotional and behavioural responses influence cognitive appraisals about the voices (Chadwick & Birchwood, 1994; Mawson, Cohen, & Berry, 2010; Morrison & Haddock, 1997; Morrison, Haddock, & Tarrier, 1995). The experience of an auditory hallucination has been suggested to occur when an individual misattributes some internal stimuli (e.g., unwanted intrusive thoughts), to an external source (Morrison & Haddock, 1997; Morrison et al., 1995). The proposed mechanism of change resulting from CBT is through changing beliefs about voices, thereby reducing distress, as well as enhancing effective coping strategies (Ruddle, Mason, & Wykes, 2011). Although evidence of the effectiveness of CBT to specifically target auditory verbal hallucinations is growing, individual CBT for voices remains costly, and demands typically exceed available resources. A good alternative to individual therapy is group therapy, as it is cost-effective, provides a place for patients to relate to other's experiences and to feel less stigmatized and more accepted, and helps to improve social functioning (Goodliffe, Hayward, Brown, Turton, & Dannahy, 2010; Lecomte et al., 2008; McLeod, Morris, Birchwood, & Dovey, 2007a). Three randomized controlled trials (RCTs) of group CBT for voices (CBTv) have been conducted. An RCT comparing group CBTv to treatment as usual (TAU) with a sample size of 85 outpatients found significant improvements in social functioning for up to six months after the end of group CBTv, as well as some improvement in self-esteem and effective coping strategies (Wykes et al., 2005). Another RCT demonstrated a significant reduction in voice frequency and in perceived voice power, as well as a trend towards distress reduction, and at a much lower cost than individual therapy (McLeod, Morris, Birchwood, & Dovey, 2007a, 2007b). A third RCT compared group CBTv to a treatment consisting of supportive therapy and found significant improvements in general symptoms and positive symptoms (Penn et al., 2009).

Neuroimaging studies suggest that psychotherapy can lead to lasting structural changes in brain regions that are important for effective information processing (see Weingarten & Strauman, 2015 for review). Studies have documented neural changes following CBT for a number of psychological illnesses (e.g.,

depression (Fu et al., 2008), obsessive-compulsive disorder (Schwartz, Stoessel, Baxter, Martin, & Phelps, 1996), panic disorder (Prasko et al., 2004), social anxiety (Furmark et al., 2002), and specific anxiety (Schienle, Schäfer, Stark, & Vaitl, 2009). Two fMRI studies have examined neural changes following CBT treatment of psychosis (Kumari et al., 2010, 2011). Of the two studies, only one explored changes in face processing following a course of CBTp (Kumari et al., 2011). The authors examined functional brain changes following CBT for psychosis in patients with persistent and distressing positive symptoms of schizophrenia. Participants completed an implicit affective processing task with stimuli depicting facial emotions of fear, anger, happiness, or neutrality. Following treatment, patients in the CBTp group showed a decrease in activation in a number of regions (e.g., inferior frontal lobe, insula, thalamus, occipital lobe) during the processing of angry and fearful facial expressions. The authors suggested that their study was the first to provide evidence that CBTp attenuates brain responses to threatening stimuli. They also suggested that the treatment may mediate symptom reduction by promoting the processing of threats in a less distressing way.

Using electrophysiological measures, such as event-related potentials (ERPs), is an effective way to assess various levels of perceptual and cognitive processing. ERPs provide direct and non-invasive measurements of electrical activity in the brain. They are recorded through the scalp at the time of a response, leading to excellent temporal resolution (Woodman, 2010) allowing for measurement of brain activity from one millisecond to the next. ERPs result from averaging time-sequences of electroencephalogram (EEG) data that is time-locked to an event, such as the presentation of a stimulus or the execution of a manual response. ERPs are embedded in the EEG signals and their extraction requires averaging of raw EEG data across many repetitions of the same type of trials (as well as other signal cleaning measures). When averaged in this way, an ERP waveform/peak is unmasked with a positive (P) or negative (N) deflection. ERPs are categorized according to their polarity (positive or negative going voltage), scalp distribution, and latency following stimulus presentation. Electrophysiological studies of face recognition have revealed a number of ERP components associated with face recognition that can be used to investigate the time-course and stages of face processing: P100, N170, and P300 (Earls, Curran, & Mittal, 2015; Hinojosa, Mercado, & Carretié, 2015; Turetsky et al., 2008). The P100 is one of the earliest components thought to reflect initial visual information processing and index automatic attention allocation (Luck et al., 1994). The N170 component is thought to represent the earliest stage of facial

structure encoding (Herrmann, Ehlis, Ellgring, & Fallgatter, 2005). Finally, the P300 component is believed to reflect higher-level cognitive processing, including stimulus evaluation and selection, and is believed to index the affect encoding stage in processing emotions (An et al., 2003).

The P100 (Earls, Curran, & Mittal, 2015), N170 (Hinojosa, Mercado, & Carretié, 2015), and P300 (Shah et al., 2018; Turetsky et al., 2008) have all been reported to be impaired in patients with schizophrenia relative to controls (Earls, Curran, & Mittal, 2015; McCleery et al., 2015; Turetsky et al., 2008). Several studies have shown smaller or delayed ERP amplitudes in patients with schizophrenia to facial emotion recognition or face perception tasks (McCleery et al., 2015; Earls, Curran, & Mittal, 2015), suggesting reduced and delayed attention allocation (engagement) to face and facial emotion stimuli.

Researchers have suggested that experiencing auditory hallucinations interferes with processing in both auditory and visual modalities (Bruder et al., 2011; van Lutterveld, Sommer, & Ford, 2011). Kayser and his colleagues (2012) examined whether patients' tendency to experience auditory hallucinations affects early visual processing. The authors found that patients who reported experiencing auditory hallucinations had substantially reduced N170 to faces compared to controls and non-hallucinators, suggesting that the association between hearing voices and impaired auditory processing is not limited to the auditory modality but also extends to impairment in visual processing, particularly face processing (Kayser et al., 2012). Thus, patients with auditory hallucinations show increased distress over hearing voices as well as experience impairments secondary to the positive symptoms (i.e., impaired early visual processing).

The Present Study

Group CBTv for schizophrenia has been shown to reduce overall symptoms, including distress associated with auditory hallucinations. Also, it has been shown to improve social functioning (McLeod et al., 2007a, 2007b; Penn et al., 2009; Wykes et al., 2005). Although there is evidence of CBTv's effectiveness in schizophrenia patients, no researchers, to our knowledge, have investigated if CBTv affects the electrophysiological markers of schizophrenia. The aim of the present study was to observe, for the first time, what kind of neural changes, if any, might emerge following CBTv in patients with persistent and distressing positive symptoms—specifically auditory verbal hallucinations. This was done by testing whether ERPs elicited by facial expressions were altered in patients with schizophrenia following

completion of CBTv. Auditory verbal hallucinations are thought to be related to attentional processing (Ensum & Morrison, 2003; Morrison & Haddock, 1997). The CBTv treatment protocol used in the present study aimed to reduce emotional salience and distress associated with hearing voices, which in turn, was expected to increase focus on external rather than internal stimuli (voices) resulting in improved cognitive and social functioning, as measured by face processing. Measuring ERPs pre- and post-therapy allowed us to observe any underlying neurophysiological changes that arose as a result of CBTv intervention.

The participants in the treatment group underwent CBTv group therapy, which was designed to be especially effective in helping patients cope with auditory hallucinations. The pre-post data from the CBTv treatment group and TAU group were compared. Participants in the TAU group continued to receive their usual treatment that included psychiatric medication and doctors' appointments. As the therapy intervention aims to reduce distress related to auditory hallucinations and improve functioning, only patients with schizophrenia who reported experiencing auditory verbal hallucinations were included in the study. The CBTv administered an integrated Attention Training Technique (ATT; Wells, 1990) and Acceptance and Commitment Therapy (ACT; Bach & Hayes, 2002) with the goal of reducing the emotional salience and distress associated with voices. ATT requires participants to listen to sounds and to systematically apply selective attention, attention switching, and divided attention. The ATT was integrated into group CBTv to reduce the attention capture of voices, in turn, decreasing ruminative processing and negative affect. The technique is aimed at enhancing executive control and learning that the control of attention is independent of internal and external events (Carter & Wells, 2018). ACT incorporates acceptance, mindfulness, and values clarification techniques to facilitate traditional behavioural interventions by focusing on modifying the patient's relationship with their thinking. Specifically, ACT aims to accept and experience internal events with a non-judgmental stance, while, at the same time, working toward reaching behavioural goals (Gaudiano & Herbert, 2006; Hayes, Strosahl, & Wilson, 1999). The goal of CBTv with ATT and ACT interventions was to reduce the emotional salience and distress associated with voices. The resulting reduction in perceived threat of the voices with CBTv (integrating ATT and ACT interventions) was expected to allow for greater focus on external rather than internal stimuli (i.e., voices), hence positively impacting cognitive and daily functioning. Following completion of CBTv, we expected to observe larger P100 and N170 amplitudes and P300 mean activity

and shorter P100 and N170 latencies in response to facial expressions. Changes in P100, N170 amplitudes, and P300 mean activity following completion of CBTv would reflect improvement (increased brain activation) in early visual information processing, facial encoding and affect encoding, respectively. Changes in P100 and N170 latencies following CBTv would reflect improvement (earlier/faster brain activation) of early visual information processing and facial encoding, respectively. We also hypothesized that we would observe reduced clinical ratings of hallucinatory activity (as evidenced by the *Psychotic Symptom Rating Scale* and *Positive and Negative Syndrome Scale* scores) and an improvement in accuracy scores on the social cognition measure MiniPONS (Short Multichannel Version of the *Profile of Nonverbal Sensitivity*). Finally, we predicted an improvement in accuracy scores and reaction times in categorizing facial expressions. We did not expect to observe any changes in these measures following the wait time period in the TAU group. Our prior work comparing facial processing in this sample of patients and healthy controls revealed a general impairment in facial expression processing across five basic emotions (neutral, joy, sad, fear, anger; Shah et al., 2018). Based on our findings from prior work, we did not hypothesize a change in the processing of any one particular emotional expression or group of expressions and did not include an emotional expression factor in our analyses.

Method

Participants

The study was approved by the Research Ethics Boards of the Royal Ottawa Mental Health Centre and the University of Ottawa. Informed consent was obtained from all participants prior to participation. The study involved 25 individuals (10 women, 15 men) with schizophrenia (SCZ; $M = 45.95$ years, $SD = 12.60$), who were diagnosed by trained psychiatrists using the *Structural Clinical Interview DSM-IV-TR* (SCID-I). All participants included met these inclusion criteria: 1) being between the ages of 18 and 60; 2) having a consistent history of auditory verbal hallucinations over the course of their illness; 3) in the *Positive and Negative Symptoms Scale* (PANSS; Kay, Fiszbein, & Opler, 1987), having a score greater than 3 on the hallucination item of the *Positive Symptom Scale* (reflecting mild or greater auditory/verbal hallucinatory experience) and less than 65 on the total score (to screen out individuals with severe level of symptoms and severe impaired functioning that would impact their ability to participate in group CBTv); 4) having no history of neurological conditions or head injury; 5) being clinically stable, as indicated by no significant change in symptoms or medication, for at

least the last three months prior to testing; 6) having included in their primary medication one of the atypical antipsychotics; and 7) being willing to participate in five-six months of CBT for voices group therapy in addition to their usual treatment. Of note, participants were not asked about the use of general anesthesia, as such the use of general anesthesia was not controlled for. All participants filled out the PANSS and the *Global Assessment of Functioning* (GAF; American Psychiatric Association, 2000).

Nineteen adult controls (8 women, 11 men) with no psychiatric history were also assessed. Healthy controls (HC) were matched to the patient group with regards to gender, age and education level. Control participants were interviewed by a trained investigator to ensure absence of these exclusion criteria: psychopathology, alcohol or drug abuse (assessed with an adaptation of the *Structured Clinical Interview, Non-Patient* version [SCID-I/NP]; First, Spitzer, Gibbon, & Williams, 1996), history of seizures, history of significant brain trauma, known anatomical brain lesions, or presence of schizophrenia history in a first-degree relative. HCs completed the *Beck Depression Inventory-II* (BDI-II; Beck, Steer, & Brown, 1996) and the *Beck Anxiety Inventory* (BAI; Beck, Epstein, Brown, & Steer, 1988). A hearing test was also administered and those who exhibited a hearing loss greater than 30 dB SPL were excluded from study participation. Participants with refractive errors were required to correct their vision with glasses while undergoing the study assessments. Of note, the researchers did not control for strabismus or colour-blindness.

Study Design

Of the twenty-five patients recruited, fourteen patients (eight males) received CBT for voices

(CBTv) group therapy for five-six months in addition to their usual treatment (CBTv+TAU group) and eleven (seven males) continued their treatment as usual (TAU-only group). The patients in both groups were recruited from the Outpatient Schizophrenia Program of the Royal Ottawa Mental Health Centre and randomly assigned to one of the two groups. The patients in the study followed a randomized parallel group design. The recruitment and creation of groups were made following these steps: 1) a patient referral through a hospital psychiatrist to the study team; 2) the introduction of the study requirements and involvement by the study team and consent from participants; 3) completion of screening session to ensure patients met the study requirements; 4) recruitment into the CBTv+TAU group based on clinical suitability; and 5) recruitment into the TAU-only group based on similar demographic and clinical characteristics. Groups were matched with respect to clinical history (duration of illness, number of episodes/hospitalizations), medication, PANSS score, Auditory Hallucinations subscale of the *Psychotic Symptom Rating Scale* ratings (PSYRATS; Haddock, McCarron, Tarrier, & Faragher, 1999), age, education level and gender. Patients in the CBTv+TAU group received CBTv for five-six months, while patients in the TAU-only group were followed for five-six months during the study. This group then received CBTv treatment for five-six months. Patient assessments were compared with HC tested on the same experiments but assessed only once. Refer to Figure 1 for the study outline schematic.

Of the fourteen patients recruited in the CBTv+TAU group, eleven patients (six males) completed all assessments at baseline and follow-up and provided usable EEG data. Of the eleven patients recruited in the TAU-only group, nine (five males)

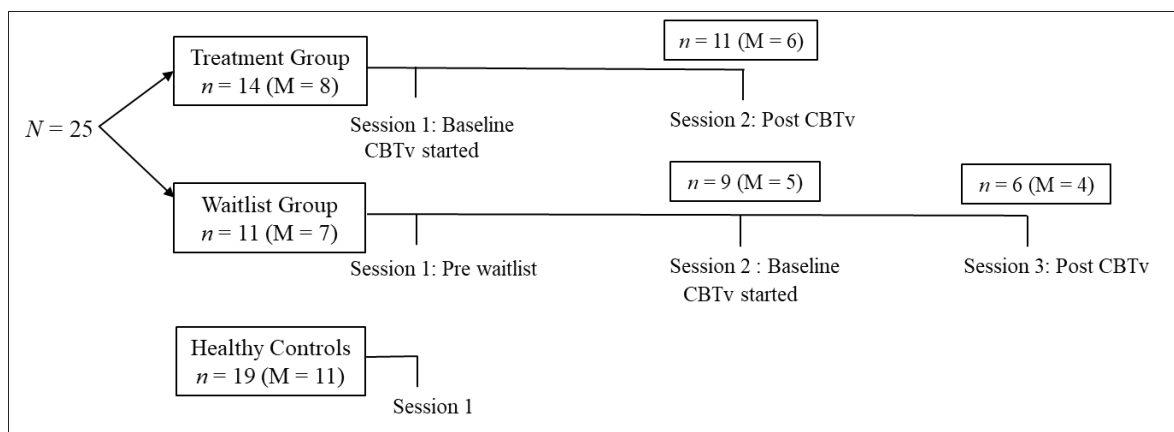


Figure 1. Study design with number of participants in each group at the beginning and after completing all study assessment. M: number of males in the group.

completed all assessments at baseline and follow-up and provided usable EEG data. The TAU-only group also received CBTv+TAU following completion of their TAU-only group period. Thus, five patients dropped out or provided unusable data, resulting in an attrition rate of 20%. Of the nine patients who completed the TAU-only group, six completed all assessment at baseline, follow-up and post CBTv and provided usable EEG data. Throughout the study, patients continued with their regular medication and psychosocial interventions. These patients dropped or were excluded for these following reasons: 1) consent withdrawal; 2) incomplete or unusable EEG data at both time points (e.g., noisy EEG data, less than 40 epochs per condition, data with missing channels, and/or incomplete task); 3) medication change; and 4) onset of medical illness. Table 1 shows clinical and demographic characteristics of the final patient samples in both groups. Study sessions consisted of obtaining assessment of mood, psychotic symptoms, and social cognitive functioning. Also, most importantly for the current study, EEG activity during an emotional facial identification task was measured.

The final CBTv+TAU and TAU-only groups were similar in age, gender, years of education, duration of illness, and all clinical symptom scores (BDI, BAI, PANSS positive items, PANSS negative items, PANSS total score, and PSYRATS total score). Accuracy scores and reaction times to respond to facial expressions were also similar between the CBTv+TAU and TAU groups. Table 1 provides means and standard deviations for both groups.

Cognitive Behavioural Therapy for Voices (CBTv) Protocol

Consistent with the NICE and PORT guidelines (Kreyenbuhl, Buchanan, Dickerson, & Dixon, 2010; NCCMH, 2009), group CBTv was delivered using a manualized approach. A manualized approach is one where prescribed goals and techniques to be used during treatment sessions are outlined and followed throughout treatment. This was done in eighteen planned sessions over five months, facilitated by highly trained group leaders. The CBTv intervention incorporated CBT strategies for positive symptoms and ATT as well as ACT within a CBT framework. Each participant was given a copy of the participant manual, which included all homework/practice assignments. The eighteen session CBTv group was administered on a weekly basis for five months (during the last two months, sessions were spread out to every two weeks). Each CBTv group had approximately nine participants. Adherence to the CBTv protocol across the groups was assessed by adherence to the treatment manual and measured by

the *Cognitive Therapy Scale for Psychosis (CTS-Psy; Haddock et al., 2001)*.

Symptom Assessment

Patients were assessed independently at two test sessions: at baseline and at the end of therapy (five months after baseline). The TAU-only group was assessed at three test sessions: baseline, at the end of the waitlist period (five months after baseline) and at the end of therapy (ten months after baseline). The MiniPONS was administered during the test sessions to measure social cognition skills. The following primary CBTv outcome measures were implemented:

Positive and Negative Syndrome Scale (PANSS). The Structured Clinical Interview for the PANSS (Kay et al., 1987) is a 30-item rating scale designed to measure the presence and severity of psychopathology in patients with schizophrenia, schizoaffective disorder, and other psychological disorders. The PANSS was completed by a trained clinician following a semi-structured interview format and using available clinical information. The clinician was blind to the group assignments. Each item was rated by the clinician on a Likert scale ranging from 1 (*not present*) to 7 (*extremely severe*). Three subscales scores were derived: *Positive Symptoms* scores (possible range of scores: 9-49); *Negative Symptoms* scores (possible range of scores: 7-49) and *General Symptoms* Scores (possible range of scores: 16-112).

The Psychotic Symptom Rating Scales (PSYRATS). The PSYRATS (Haddock, McCarron, Tarrier, & Faragher, 1999) includes two scales designed to measure the severity of a number of dimensions of auditory hallucinations and delusions. Only the *Auditory Hallucinations* subscale was administered to the patients, which includes an 11-item scale that assesses dimensions of auditory hallucinations. The items include frequency, duration, location, loudness, amount and intensity of distress, amount and intensity of negative content, disruption, controllability, and number of voices. Symptoms scores are rated on a 5-point ordinal scale (0-4).

Global Assessment of Functioning (GAF). The GAF (American Psychiatric Association, 2000) was used to rate the patients' social, occupational, and psychological functioning. The GAF is an overall measure of how patients are doing and can be useful in tracking the clinical progress of individuals in global terms. The GAF scores range from 1-100, where lower scores indicate reduced functioning and higher scores indicate that the patient is not in need of therapy. The GAF was completed by a trained clinician, who was blind to the group assignments.

Table 1
Demographics, clinical characteristics and task performance data of patients and HCs

	CBTv+TAU group		TAU-only group		HC
	<i>(n = 11; 6 males)</i>		<i>(n = 9; 5 males)</i>		<i>(n = 19; 11 males)</i>
	<i>M (SD)</i> <i>Baseline</i>	<i>M (SD)</i> <i>Follow-up</i>	<i>M (SD)</i> <i>Baseline</i>	<i>M (SD)</i> <i>Follow-up</i>	<i>M (SD)</i>
Demographics					
Age (years)	44.82 (13.82)		48.78 (12.09)		47.00 (7.97)
Education (Years)	4.64 (1.43)		5.50 (1.18)		5.37 (1.38)
Duration of illness (Years)	18.88 (11.39)		21.78 (9.60)		
BDI	10.46 (8.18)	9.09 (7.80)	16.60 (16.29)	16.50 (14.38)	4.97 (4.77)
BAI	20.91 (13.03)	16.82 (14.14)	22.20 (14.74)	19.00 (13.54)	3.95 (4.28)
MiniPONS %	60.14 (9.30)	59.31 (11.10)	65.63 (7.76)	64.24 (6.02)	76.55 (1.47)
GAF ^a	46.00 (9.22)	50.10 (7.65)	44.60 (11.84)	52.86 (17.17)	
PSYRATS	25.09 (5.77)	22.64 (6.80)	27.50 (4.62)	27.40 (5.99)	
PANNS^b					
Positive Scale	15.45 (4.83)	15.80 (5.06)	15.60 (3.74)	16.71 (5.74)	
Negative Scale	15.82 (4.83)	15.20 (4.16)	15.33 (4.39)	14.43 (4.86)	
General Psychopathology	33.54 (4.90)	28.80 (4.51)	31.33 (6.79)	28.43 (9.27)	
Performance Emotion identification accuracy (%)					
Neutral	63.79 (32.36)	69.46 (30.01)	59.47 (34.65)	62.60 (38.58)	70.39 (26.98)
Joyful	85.29 (9.32)	84.03 (24.18)	89.04 (14.73)	74.98 (35.73)	94.35 (18.17)
Sad	69.77 (2.74)	60.75 (23.85)	58.99 (20.09)	70.92 (19.34)	73.21 (24.41)
Angry	75.43 (4.66)	74.55 (31.18)	67.36 (19.82)	65.42 (36.06)	88.68 (14.42)
Fearful	75.21 (8.98)	74.30 (24.18)	82.00 (14.76)	77.75 (26.86)	88.84 (18.33)

Note. PSYRATS: *The Auditory Hallucinations subscale from the Psychotic Symptom Rating Scale*; PANNS: *Positive and Negative Syndrome Scale*; MiniPONS: *Short Multichannel*

^{a,b} follow-up for the GAF and PANNS measures included missing data (one missing case for the CBT + TAU group and three missing cases for the TAU-only group).

Beliefs About Voices Questionnaire-Revised (BAVQ-R). The BAVQ-R (Chadwick, Lee, & Birchwood, 2000; Appendix I) is a 35-item self-report questionnaire that measures perceptual, emotional and behavioural responses to auditory verbal hallucinations. The items are rated on a 4-point scale ranging from 0 (*disagree*) to 4 (*strongly agree*). The questionnaire consists of five subscales measuring different meanings given to the voices: *omnipotence* with six items (e.g., *My voice is very powerful*), *malevolence* with six items (e.g., *My voice is persecuting me for no good reason*), *resistance* with nine items (four items for *emotion* (e.g., *My voice frightens me*), and five items for *behaviour* (e.g., *When I hear my voice usually I tell it to leave me alone*)), *benevolence* with six items (e.g., *My voice wants to help me*) and *engagement* with eight items (four for *emotion* (e.g., *My voice makes me feel calm*) and four for *behaviour* (e.g., *I seek the advice of my voice*)).

The Short Multichannel Version of the Profile of Nonverbal Sensitivity (MiniPONS). The MiniPONS (Bänziger, Scherer, Hall, & Rosenthal, 2011) was used to assess social cognition, which is the ability to recognize the communication of feelings, attitudes, and intentions from nonverbal expression in faces, voices, gestures, and body postures. The MiniPONS correlates highly with the full version and has shown construct validity through significant correlations with other tests of emotion recognition ability (Bänziger et al., 2011). The shorter version of the Pons was used to account for the limited time during test sessions. A series of 64 two-second video clips of a Caucasian female were used in the MiniPONS. Each scene contained, either singly or in combination, facial expressions, voice intonations, and bodily gestures. After watching each scene, the participants were asked which of two labels (e.g., *talking to a child* or *saying a prayer*) best described the scene. A practice session was administered with three supplement scenes to ensure participants understood the task. The percentage of correct responses was used as the dependent measure.

EEG Session Procedures

Upon arrival at the laboratory, all participants were administered the MiniPONS. Only the patients were administered the PSYRATS. Electrodes were applied to the participant's scalp and face, from which EEG activity was recorded while completing the emotional facial identification task.

Emotional Facial Identification Task

Stimuli. A detailed description of the stimuli used for the study can be found in Shah et al. (2018). Facial expression stimuli were derived from Gosselin,

Kirouac, and Doré (1995). Each facial expression was displayed by four actors (two female). Twenty photographic faces displaying one of five facial expressions (four joyful, four angry, four fearful, four sad, and four neutral) were used. Each facial expression image was presented 17 times, yielding a total of 340 trials with facial expression stimuli. In addition to face stimuli, four different chair photographs were used as control stimuli and each chair photograph was presented 17 times for a total of 68 trials with chair stimuli. Altogether, there were 408 trials (340 with faces and 68 with chairs). All photographs were digitized and converted to grey-scale images and matched for luminance and contrast. Neck and background were cropped out and the face stimuli were trimmed into rectangles.

Emotional Facial Identification Task Procedures. During the task, all participants were seated in a comfortable chair and viewed all stimuli presented on a 17-inch computer screen positioned approximately 1 m in front of the seated participant in a dark room. Each grey-scale picture of a neutral, joyful, fearful, angry, or sad facial expression, as well as each chair stimulus, was presented a total of 68 times. Trials were presented in random order. Three rest periods were given, one after each quarter of the trials had been completed. Each trial began with a fixation cross (200ms), followed by a face or chair stimulus (500ms). For 120 of the trials, the face or chair stimulus was followed by a response prompt asking the participant to identify the emotion being expressed via a key press. A blank screen appeared between trials (ITI = 800-1,000 ms). An equal number of trials requiring a response appeared for each stimulus type (i.e., 20 for each facial expression and 20 for the chairs). Participants' responses and reaction times (RT) were recorded automatically. Responses were requested for chair stimuli as well as face stimuli, even though the chairs would not normally be said to express an emotion.

Electrophysiological Recordings and Data Reduction

During the emotional facial identification task, continuous EEG activity was recorded with a cap embedded with Ag+/Ag+-Cl ring electrodes (EasyCap®, Herrsching-Breitbrunn, Germany) at 32 scalp sites positioned according to the 10-10 system of electrode placement. Additional electrodes were placed on the orbital ridges and external canthi of the eyes to monitor vertical and horizontal electrooculographic (EOG) activity and subsequently minimize contamination from eye movements and blinks. Linked electrodes positioned at the left and right mastoids served as the reference and a frontally positioned electrode served as the ground. Electrode

impedances were kept below 5 K Ω and EEG activity was digitally sampled at 500 Hz (BrainVision Recorder®, Richardson, TX, USA). The electrical signals were amplified with a bandwidth filter set at 0.1-80 Hz and stored on a hard disk for subsequent off-line processing and analysis (BrainVision Recorder®, Richardson, TX, USA).

Off-line EEG data analysis was carried out using BrainVision Analyzer 2 (BrainVision Analyzer®, Richardson, TX, USA). During off-line signal processing, analytical procedures were applied to the stored digitized recordings: 1) individual trials were filtered at 0.1-30.0 Hz; 2) an ocular correction software algorithm (Gratton, Coles, & Donchin, 1983) was employed to correct for the effects of eye movements and blinks based on the EOG recordings; 3) Data was segmented into 1,600 ms epochs for each stimulus, with a timespan from 100 ms pre-stimulus onset to 1,500 ms post-stimulus onset. Epochs with responses were pooled with those without responses; 4) trial epochs with EEG voltages greater than $\pm 75\mu\text{V}$ were removed; 5) filtered epochs were baseline corrected by subtracting averaged electrical activity 100 ms prior to stimulus onset; and 6) codes synchronized with stimulus delivery were used to average together epochs associated with the different stimulus categories (i.e., angry, fearful, joyful, neutral, and sad faces, plus chairs).

ERP Analysis

ERPs were identified based on visual examination of grand-averaged waveforms and previous literature (Campanella, Montedoro, Streeb, Verbanck, & Rosier, 2006; Jung, Kim, Kim, Im, & Lee, 2012; Lee, Kim, Kim, & Bae, 2010; Luo, Feng, He, Wang, & Luo, 2010; Turetsky et al., 2007; Wynn, Lee, Horan, & Green, 2008). The following components were identified for facial expressions and chair stimuli: P100 (measured at P_{7/8} and O_{1/2}; with maximum positive voltage within the time window of 80-130 ms following face stimulus onset), N170 (measured at P_{7/8}; with maximum negative voltage within the time window of 140-230 ms following stimulus onset), and P300 (measured at P_z with mean positive activity within the time window of 200-600 ms). All peak amplitudes and mean amplitudes were measured relative to mean pre-stimulus voltage levels. Peak latencies of the P100 and N170 (i.e., time to reach maximum voltage) were assessed relative to stimulus onset.

Statistical Analysis

CBTv+TAU compared with TAU-only groups: baseline comparisons. Independent samples t-tests were used to compare the final CBTv+TAU and TAU-only groups at baseline on age, gender, education,

MiniPONS scores, and clinical symptoms scores (PANSS, PSYRATS, GAF, BDI and BAI). Independent samples t-tests were also used to compare behavioural performance indices (accuracy and median RT) across groups. These were calculated regarding the identification of all facial expressions (i.e., accuracy for joyful, angry, sad, fearful and neutral face stimuli collapsed together). An alpha level of .05 for testing significance was maintained.

Effects of CBTv: Symptom, accuracy and ERP changes in CBTv+TAU compared TAU groups. CBTv treatment changes in clinical symptom (PANSS, GAF, PSYRATS and PSYRATS items) and social cognition (MiniPONS) scores were analyzed using paired-samples t-tests for both the CBT+TAU and TAU-only groups. Behavioural performance (accuracy and median RT) data was analyzed with mixed repeated measures ANOVA using group (CBTv+TAU and TAU-only) as a between-subjects factor and time (baseline and follow-up) as within-subjects factor.

P100 amplitude and latency data were analyzed with mixed repeated measures ANOVA using group (CBTv+TAU and TAU-only) as a between-subjects factor and site (occipital, parietal), hemisphere (right, left) and time (baseline, follow-up) as within-subjects factors. N170 amplitude and latency data were analyzed with mixed repeated measures ANOVA using group (CBTv+TAU and TAU-only) as a between-subjects factor and hemisphere (right, left) and time (baseline, follow-up) as within-subjects factors. P300 mean activity data was analyzed with mixed repeated measures ANOVA using group (CBTv+TAU and TAU-only) as a between-subjects factor and time (baseline, follow-up) as within-subjects factors. Significant main effects or interactions involving the group factor were followed up by within-subjects ANOVAs for each group. An alpha level of .05 for testing significance was maintained.

Patient group compared with healthy participants. We tested for differences between the patient group (at baseline) and the healthy control group in age, education, clinical symptom scores (BDI and BAI), and MiniPONS accuracy scores using independent samples t-tests. Similar comparisons regarding performance were tested for using an ANOVA with Group (SCZ, HC) as the between-subjects variable and facial expression (fearful, joyful, sad, angry and neutral) as the within-subjects variable. Group differences in ERP responses to facial expressions between patients (at baseline) and healthy controls were also tested for with repeated-measures ANOVAs. These had group (SCZ, HC) as the between-subject variable and facial expression (fearful, joyful,

sad, angry and neutral), hemisphere (right, left: for P100 and N170) and site (parietal, occipital: only for P100) as within-subjects variables. The error terms from the ANOVA were used to conduct planned contrasts (Rosenthal & Rosnow, 1985) to test study hypotheses (Shah et al., 2018).

Results

Patient Group Compared with Healthy Participants

The detailed results of these ANOVAs can be found in Shah et al. (2018), but in summary, patients with schizophrenia were slower at identifying all facial expressions, including neutral ones. They also showed smaller P100 amplitude to sad, angry, and fearful facial expressions relative to healthy controls. N170 amplitude was smaller in patients in response to neutral, joyful, angry, and fearful facial expressions. Patients showed smaller P300 mean amplitudes to all facial expressions, including neutral ones.

Effects of CBTv: Task Performance and Symptom Scores

The ANOVA revealed no changes in accuracy scores or reaction time in facial expression categorization at follow-up (post-treatment) compared to baseline (pre-treatment) in either the CBTv+TAU or TAU-only groups ($F < 1$ for Group, and Group x Time). Paired-sample *t*-tests were conducted to test for changes in symptom scores and MiniPONS accuracy scores between baseline (pre-treatment) and follow-up (post-treatment) in both the CBTv+TAU and the TAU-only groups. There were no significant differences in symptom scores from baseline to follow-up for GAF, PANSS-positive, and PSYRATS-total scores.

CBTv+TAU group

PSYRATS items. The paired sample *t*-test for the CBT+TAU revealed a significant difference across testing sessions in the score for one of the PSYRATS items: “amount of negative content”, where the treatment group reported a reduced amount of negative content in their voices following group CBTv treatment ($M = 2.18$, $SD = 1.17$) relative to baseline ($M = 3.00$, $SD = 0.89$); $t(10) = 2.76$, $p = .02$. The treatment group also showed a trend towards reduction in the “loudness of auditory hallucinations” following group CBTv treatment ($M = 1.73$, $SD = .65$) relative to baseline ($M = 2.18$, $SD = 0.75$); $t(10) = 1.84$, $p = .09$.

BAVQ-R. A significantly improved BAVQ-R subscale *omnipotence* score was observed in the CBTv+TAU group following group CBTv treatment ($M = 4.64$, $SD = 5.66$) relative to baseline ($M = 7.00$, $SD = 5.16$); $t(10) = 2.34$, $p = .04$. A trend towards improvement in the *resistance-behaviour* subscale

following group CBTv treatment ($M = 10.64$, $SD = 4.46$) relative to baseline ($M = 8.73$, $SD = 4.96$); $t(10) = -1.92$, $p = .08$ was also observed.

MiniPONS. A trend towards improvement in MiniPONS accuracy scores following group CBTv treatment ($M = 64.69\%$, $SD = 11.27$) relative to baseline ($M = 59.31\%$, $SD = 11.10$); $t(9) = -1.96$, $p = .08$ was observed.

TAU-Only Group

The significant differences reported above in the CBTv+TAU group following treatment were not observed in the TAU-only group. However, the TAU-only group did reveal a trend towards reduction of PANSS negative scores $t(5) = 2.45$, $p = .06$, and a trend towards improvement of the BAVQ-R subscale *benevolence* $t(8) = -2.18$, $p = .06$ at follow-up (PANSS negative: $M = 14.00$, $SD = 5.17$; BAVQ-R *benevolence*: $M = 5.44$, $SD = 4.80$) relative to baseline (PANSS negative: $M = 16.00$, $SD = 3.69$; BAVQ-R *benevolence*: $M = 2.56$, $SD = 3.47$).

Effects of CBTv: ERP Changes Following CBTv

P100 Amplitude and Latency. The P100 amplitude mixed repeated measures ANOVA revealed significant site by group $F(1, 18) = 5.07$, $p = .04$, $\eta_p^2 = .22$ and time by hemisphere by group $F(1, 18) = 6.19$, $p = .02$, $\eta_p^2 = .26$ interactions. A follow-up ANOVA within the CBTv+TAU group showed significant time by hemisphere $F(1, 10) = 5.97$, $p = .04$, $\eta_p^2 = .37$ and site by hemisphere interactions $F(1, 10) = 10.03$, $p = .01$, $\eta_p^2 = .50$. Follow-up pairwise comparisons of the time by hemisphere interaction revealed larger P100 amplitude over the right ($M = 5.05 \mu V$, $SD = 2.61$) compared with the left ($M = 3.75 \mu V$, $SD = 1.34$) hemisphere at follow-up, $p = .02$.

A follow-up ANOVA within the TAU-only group showed a significant interaction of time by site $F(1, 8) = 10.52$, $p = .01$, $\eta_p^2 = .57$. Follow-up pairwise comparison of the time by site interaction revealed larger P100 amplitude over the occipital ($M = 5.53 \mu V$, $SD = 3.17$) relative to the parietal ($M = 4.03 \mu V$, $SD = 2.31$) site at follow-up, $p = .009$. Neither the CBTv+TAU nor the TAU-only group showed a P100 amplitude treatment effect.

The P100 latency mixed repeated measures ANOVA revealed significant time by group interaction $F(1, 18) = 14.51$, $p = .001$, $\eta_p^2 = .45$. A follow-up ANOVA within the CBTv+TAU group showed significantly shorter P100 latency following completion of group CBTv $F(1, 10) = 19.68$, $p = .001$, $\eta_p^2 = .66$ ($M = 109.48$ ms, $SD = 7.11$) compared with baseline ($M = 114.44$ ms, $SD = 7.54$; c.f. Figure 2). A

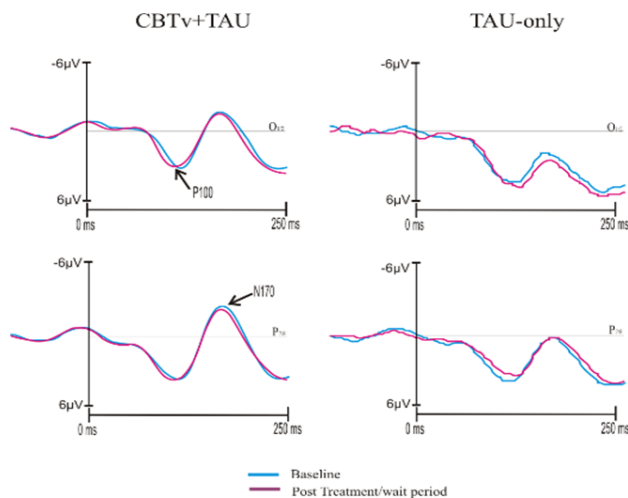


Figure 2. P100 and N170 grand averaged waveforms in response to facial expressions measured at baseline and following CBTv treatment or wait period. P100 is measured over occipital site (O_1 and O_2 pooled), N170 is measured over parietal sites (P_7 and P_8 pooled).

similar follow-up ANOVA within the TAU-only group did not show any significant main or interaction effects.

N170 Amplitude and Latency. The N170 amplitude mixed repeated measures ANOVA revealed significantly larger amplitude $F(1, 18) = 10.12$, $p = .005$, $\eta_p^2 = .67$, in the CBTv+TAU group ($M = -3.34 \mu\text{V}$, $SD = .75$) compared with the TAU-only group ($M = -0.40 \mu\text{V}$, $SD = .17$). The N170 latency mixed repeated measures ANOVA revealed a significant time by hemisphere by group interaction $F(1, 18) = 7.04$, $p = .02$, $\eta_p^2 = .28$. Follow-up N170 amplitude and latency ANOVAs within the CBTv+TAU and TAU-only groups did not show any main or interaction treatment effects.

P300 Mean Amplitude. The P300 mean amplitude mixed repeated measures ANOVA did not reveal any main or interaction effects. The TAU-only group waveforms appear noisy compared with the CBTv+TAU group waveforms. A possible reason for the difference could be related to a smaller sample size in the TAU-only group ($n = 9$) relative to the CBT+TAU group ($n = 11$).

Discussion

This study was the first to investigate neural changes following five-six months of CBT for voices (CBTv) in patients with schizophrenia using ERP and an emotional facial identification task. We expected that CBTv would significantly reduce clinical ratings of hallucinatory activity found in patients with schizophrenia and improve behavioural performance

and ERP amplitudes and latencies during the emotional facial identification task.

Clinical Symptom Findings

Based on previous findings of both randomized and non-randomized controlled trials of CBTv (Gottlieb, Romeo, Penn, Mueser, & Chiko, 2013; McLoed et al., 2007a, 2007b; Wykes et al., 2008), reductions from baseline to post-treatment measures of hearing voices and related distress were predicted in the present study. These predictions were borne out. Specifically, the CBTv+TAU group reported a significantly reduced amount of negative content of voices and improved outcomes on the *omnipotence: power of voice* item of the BAVQ-R. Furthermore, the treatment group showed a trend towards reduction in loudness of voices and improved MiniPONS accuracy score following the treatment.

Contrary to our expectations, based on the findings of randomized controlled trials of CBTp and CBTv (Birchwood et al., 2014; McLoed et al., 2007a, 2007b; Penn et al., 2009; Shawyer et al., 2012; Wykes et al., 2005), the CBTv+TAU group did not show significantly reduced PANSS symptom severity, PSYRATS total scores or GAF scores at follow-up. One possible explanation for the discrepancy between our findings and those from previous studies could be related to the theoretical approach taken for the treatment and for the measurements used to test the efficacy of treatment. That is, within the general framework of CBT, different theoretical approaches may have been used in our study versus previous ones (Pontillo et al., 2016). The effects of CBT for voices have mostly been investigated by examining the efficacy of CBTp on the overall severity of positive symptoms (hallucinations and delusions combined; Thomas et al. 2014). Previous study designs involved participants experiencing a broad range of psychotic experiences (hallucinations, delusions, negative symptoms), resulting in sample heterogeneity, delivery of therapy based on a broad range of behavioural and cognitive principles, and examination outcomes using broad indices of psychological states, such as overall positive symptoms (Thomas et al., 2014). In contrast, our sample included individuals who experienced auditory verbal hallucinations and the treatment was focused specifically on beliefs about the voices' omnipotence and the patients' relationships with the voices.

The focus of CBTv is not on reducing the experience of voices or frequency and severity of symptoms, but rather on reducing the perceived power of voices and in turn the related distress experienced by patients (Birchwood & Trower, 2006). Our findings showing reduced omnipotence and negative content of voices are in line with the goal of reduced

perceived threat with CBTv as well as Birchwood and Trower's (2006) explanation of the focus of CBT treatment for voices.

Our TAU-only group showed a trend towards reduced PANSS-negative symptoms and of improvement on the BAVQ-R subscale *benevolence* from baseline to follow-up. The reason for this is unclear. One possible explanation could be related to maturation in the TAU group over the course of the study. Specifically, TAU participants may have improved their *benevolence* score on their own without treatment (e.g., participants may become more hopeful about receiving treatment). Furthermore, repeatedly completing questionnaires about their voices may have provided participants with a different view of their voices. However, these speculations are difficult to qualitatively measure. As for the difference of the TAU PANSS-negative symptom score between baseline and follow-up, it is unclear to us why this occurred, especially given that no differences emerged for electrophysiological measures, behavioural performance indices and other clinical rating scores. As such, the change in *benevolence* and PANSS-negative symptom scores in the TAU group should not discount the clinical and electrophysiological changes observed in the CBTv group. The TAU-only group showed no change in other symptoms from baseline to follow-up in any of the following: PSYRAT total, PSYRATS items, GAF, PANNS positive, PANNS general, and MiniPONS scores. This was expected given that the inclusion criteria required all patients to be clinically stable, to be on the same medication for three months prior to study entry, and to have no change in medication during the course of the study.

Behavioural and ERP Findings

Although, in our previous work, we found slower response time in categorizing all facial expressions (Shah et al., 2018) between patients with schizophrenia and healthy controls, in the current study we did not find improvement in response time following group CBTv treatment. Additionally, the CBTv+TAU group did not improve in the accuracy of categorizing facial expressions from baseline to follow-up. The CBTv+TAU and TAU-only groups displayed similar performance on the task during both sessions. These null findings are in line with Kumari et al. (2011), who found neural changes in several brain structures following CBTp that did not extend to behavioural performance improvements in the treatment group.

In line with our hypothesis, the CBTv+TAU group at follow-up showed earlier perceptual response to facial expressions, as indexed by the P100, than they did at baseline. The P100 is believed to reflect early-stage visual information processing (Luck et al., 1994;

Santesso et al., 2008) and early preconscious direction of attention (Lee, Gosselin, Wynn, & Green, 2011; Pizzagalli et al., 2002; Turetsky et al., 2007, 2008; Utama, Takemoto, Koike, & Nakamura, 2009). P100 amplitude deficits in patients with schizophrenia have been frequently reported in response to non-face and face stimuli (Earls et al., 2015; Onitsuka, Oribe, Nakamura, & Kanba, 2013; Shah et al., 2018). However, only a limited number of studies have found longer P100 latencies in patients with schizophrenia during tasks involving faces (Lee et al., 2010; Wynn et al., 2008). The longer P100 latency may be reflective of patients' general delay in processing earlier visual information (Lee et al., 2010; Wynn et al., 2008) and attending. Our study is the first to show a change in P100 latency following a course of group CBTv treatment in patients with schizophrenia. Our findings are compatible with those of Kumari and his colleagues (2011), who found reduced fMRI activation after CBTp in visual (occipital) areas, which are thought to primarily subserve early perceptual processing (Adolphs, 2002) and to receive feedback from areas processing visual emotion (Catani, Jones, Donato, & Ffytche, 2003). Of note is that the change in P100 latency did not extend to the encoding (N170) or stimulus categorization (P300) and response stages (behavioural data).

Our CBTv protocol included ATT as well as ACT interventions. ATT was included to target auditory verbal hallucinations experienced in this population. Auditory verbal hallucinations are thought to be related to attentional processing. Levels of self-focused attention predict whether or not individuals experience auditory verbal hallucinations, and thus self-focused attention is implicated in the mediation of auditory verbal hallucinations (Ensum & Morrison, 2003; Morrison & Haddock, 1997). Acceptance and mindfulness (key components of ACT) have been found to alter ERP following treatment in patients with bipolar disorder and healthy individuals (Howells, Rauch, Ives-Deliperi, Horn, & Stein, 2014; Lin, Fisher, Roberst, & Moser, 2016). ATT and ACT were integrated into group CBTv with the goal of reducing emotional salience and distress associated with hearing voices. In turn, the reduction of the perceived threat of voices with CBTv was expected to allow for a greater focus on external rather than internal stimuli (voices) and hence, impact cognitive and social functioning. Our findings of shorter P100 latency to facial expressions provide some evidence, at a neural level, of change in attention to external stimuli.

Contrary to our hypothesis, we did not observe significant changes in P100 amplitude, N170 amplitude and latency, or P300 mean activity following a course of CBTv. The reason for this is

unclear. Given that CBTv did not target perceptual training of visual stimuli, specifically facial expressions, it is plausible that the level of early sensory activity elicited by facial expression was unaltered following treatment. Seeing that there were no changes in N170 amplitude and latency and P300 mean activity, it is plausible that earlier perceptual improvements observed in the present study following CBTv did not transfer to later more conscious processing stages. Studies have shown smaller and delayed ERP amplitudes in patients with schizophrenia to facial expressions, as well as intact P100 and N170 amplitudes and latencies (Wynn et al., 2008). Furthermore, studies have reported delayed P100 latencies, but intact P100 amplitude and subsequent N170 amplitude in patients and have suggested that the pathways for the early processing of facial expression content, reflected in the P100, and the later structural encoding of facial features, reflected in the N170, are dissociable (Pourtois, Dan, Grandjean, Sander, & Vuilleumier, 2005; Pourtois, Grandjean, Sanders, & Vuilleumier, 2004; Vuilleumier & Pourtois, 2007). This could be a reason why the present study found increased efficiency in early processing and attending to visual information but did not observe any effects at later structural encoding and affect processing stages.

It is important to note the observed N170 amplitude difference between the CBTv+TAU and TAU-only group. One explanation for the difference in N170 amplitudes between groups could be that the randomization process was flawed in some way. However, this idea does not explain the insignificant differences in clinical ratings and performance scores between groups at baseline. Another explanation could be related to the effects of antipsychotic medication. Antipsychotic medication has shown effects on neural activation (Anderer, Saletu., Semlitsch, & Pascual-Marqui, 2002; Pompéia et al., 2000). Longer P100 latency during visual discrimination task has been shown following an acute dose of bromazepam (Puga et al., 2007). However, researchers have found little to no evidence to suggest that the N170 deficits reported in patients with schizophrenia stem from or are correlated with antipsychotic medication (Batty, Francis, Innes-Brown, Joshua, & Rossel, 2014; Maher, Mashboon, Ekstrom, Lukas, & Chen, 2016). The explanation for the N170 amplitude difference between our patient groups is therefore unclear, especially given that no difference emerged for P100 amplitude, behavioural performance indices and clinical rating scores at baseline. Even with the smallest N170 in the TAU-only group, relative to the CBTv+TAU group, our P100 latency effects cannot be discounted. P100 was observed prior to N170 and over both the occipital and parietal sites. As such, any

uncertainty in the N170 data should not influence the P100 data.

Study Limitations

The study was not designed primarily to test the efficacy of CBTv. Rather, the study aimed to observe changes in ERPs over the course of CBTv. As such, the task did not specifically target mechanisms involved in improved attention, mindfulness practice, or cognitive restructuring related to auditory verbal hallucinations. Furthermore, we only tested changes in processing in the visual modality. Another limitation was that we have not yet done a long-term follow-up to determine if the benefits observed in this study were sustained following completion of group CBTv. Finally, our sample size would be considered small. Future research could investigate the effects of CBTv on clinical ratings of AVH, as well as the neural responsiveness as measured with a larger sample size and range of tasks (e.g., acoustic change detection, working memory, emotional expression identification). Finally, the study did not control or gather information on anesthesia use in participants.

Of note is that our prior work (Shah et al., 2018) explored ERP responses to facial expressions in patients with schizophrenia relative to healthy controls. Our previous work showed P100, N170 amplitudes and P300 mean activity differences in groups and did not report group differences in P100 or N170 latencies. Furthermore, based on the grand averaged P100 and N170 figures, no evidence of latency differences was observed between groups. This would suggest that in our sample, patients with schizophrenia and healthy controls did not significantly differ in speed of visual information processing and that the group differences were specific to the brain's attentional activation in response to facial expressions. Thus, the results of the present study can suggest that an earlier P100 response to faces was observed following CBTv and cannot suggest that an improvement in attentional activation was observed.

Conclusion

The CBTv group showed significantly reduced amount of negative content of voices and improved outcomes on the *omnipotence: power of voice* item of the BAVQ-R. Furthermore, the treatment group showed a trend towards reduction in loudness of voices. These changes in clinical rating scores suggest a CBTv-induced alteration in beliefs about voices. Altering the beliefs about voices has been reported to reduce distress and thus enhance effective coping strategies and improve functioning (Ruddle, Mason & Wykes, 2011). Additionally, researchers also suggest that changing the relationship that patients have with

their voices, the level of social activity, and improving self-esteem may also be a recipe for improving outcomes (Ruddle et al., 2011).

Researchers have demonstrated that experiencing auditory hallucinations interferes with auditory, visual, and face processing in particular (Bruder et al., 2011; Kayser et al., 2012; van Lutterveld, Sommer & Ford, 2011). This study, to our knowledge, provides the first evidence that a course of group CBT for voices alters early perceptual processing of faces in patients with auditory verbal hallucinations. Demonstrating CBTv-induced changes to socially relevant information—faces—is important because there is a lack of knowledge about the neural mechanisms that underlie the benefits of psychotherapy (Birchwood et al., 2014; McLoed et al., 2007a, 2007b; Penn et al., 2009; Shawyer et al., 2012; Wykes et al., 2005) observed with CBT for patients with schizophrenia. The present study provides a starting point for exploring neural changes following psychotherapy in this population. Further studies should examine electrophysiological changes that accompany CBT, in particular those that reflect information processing related to specific symptoms of schizophrenia, and their effects on face and emotion processing and social cognition.

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