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Hierarchical deficits in auditory information processing in schizophrenia

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ABSTRACT

Deficits in auditory processing contribute significantly to impaired functional outcome in schizophrenia (SZ), but mediating factors remain under investigation. Here we evaluated two hierarchical components of early auditory processing: pitch-change detection (i.e. identifying if 2 tones have "same" or "different" pitch), which is preferentially associated with early auditory cortex, and serial pitch-pattern detection (i.e. identifying if 3 tones have "same" or "different" pitch, and, if "different", which one differed from the others), which depends also on auditory association regions.
Deficits in pitch-change detection deficits in SZ have been widely reported and correlated with higher auditory disturbances such as Auditory Emotion Recognition (AER). Deficits in serial pitch-pattern discrimination have been less studied. Here, we investigated both pitch perception components, along with integrity of AER in SZ patients vs. controls using behavioral paradigms. We hypothesized that the deficits could be viewed as hierarchically organized in SZ, with deficits in low-level function propagating sequentially through subsequent levels of processing.
Participants included 27 SZ and 40 controls. The magnitude of the deficits in SZ participants was large in both the pitch-change ($d = 1.15$) and serial pitch-pattern tasks ($d = 1.21$) with no significant differential task effect. The effect size of the AER deficits was extremely large ($d = 2.82$). In the SZ group, performance in both pitch tasks correlated significantly with impaired AER performance. However, a mediation analysis showed that serial pitch-pattern detection mediated the relationship between simpler pitch-change detection and AER in patients. Findings are consistent with hierarchical models of cognitive dysfunction in SZ with deficits in early information processing contributing to higher level impairments. Furthermore, findings are consistent with recent neurophysiological results suggesting similar level impairments for processing of simple vs. more complex tonal dysfunction in SZ.

1. Introduction

The notion that auditory perception is disrupted in schizophrenia (SZ) has been documented for over 20 years (review in Javitt, 2009), and has been mapped to dysfunction within early sensory, or even subcortical, auditory regions (reviewed in Javitt and Sweet, 2015). Thus, abnormal fine-grained discrimination of pitch – the auditory percept associated with sound frequency – appears to be a core feature of the illness. Furthermore, these deficits (termed "tone-matching deficits") are associated with impairments in recognizing prosody during speech, leading to deficits in correctly identifying emotion or intent (sarcasm) based upon prosody (review in Donde et al., 2017). Auditory emotion recognition (AER) and sarcasm-detection deficits, in turn, contribute to impairments in social cognition, which in turn lead to impairments in social function (Gold et al., 2012: Kantrowitz et al., 2014, 2015; Leitman et al., 2006, 2010a, 2010b, 2011).

Although much of neuroscience work treats pitch processing as a unitary concept that increases along a single dimension (Griffiths, 2003), several strands of evidence suggest that auditory tasks require a detection of different stages of change between sound frequencies. Moreover, these different stages would map, respectively, to different subregions of auditory cortex. Specifically, two hierarchical components of active frequency analysis of non-verbal tones have been dissociated: the detection of pitch change between individual notes (i.e. identifying

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if 2 tones have "same" or "different" pitch), as opposed to the change in pitch patterns such as melodies (i.e. identifying if 3 tones have "same" or "different" pitch and, if "different", which one differed from the others) (Griffiths, 2001, 2003).

The present study evaluates the relationship between two components of early auditory information processing – simple pitch-change detection and serial pitch-pattern discrimination – as mediators of AER recognition deficits in SZ.

Fine-grained discrimination of pitch is processed in humans at the level of the auditory cortex (review in Tramo et al., 2005). Early auditory regions, including primary cortex (A1), belt, and parabelt regions are encompassed by the superior temporal gyri including Heschl's gyrus and correspond mainly to Brodmann's areas BA41 (medial) and BA42 (lateral). These regions project to auditory association regions (BA 22), which are located in the anterior portion of the planum temporale and lateral superior temporal gyrus (Glasser et al., 2016; Sun et al., 2009).

Inputs to early auditory cortex arise predominantly from the medial geniculate body of the thalamus and form synapses in different cortical layers (Sherman and Guillery, 2002). Interrelated thalamic and cortical pathways are thought to support the emergence of higher auditory perception (Lee, 2013). Finally, higher order auditory processing, such as AER, is processed primarily within posterior regions of the superior temporal sulcus, as well as anterior regions such as the inferior frontal and orbito-frontal gyri in healthy volunteers (Dzafic et al., 2016; Bestelmeyer et al., 2014; Wildgruber et al., 2006; Schirmer and Kotz, 2006) and SZ patients (Kantrowitz et al., 2015; Leitman et al., 2011).

Detection of pitch-change between individual notes appears to be specifically associated to the A1 activity, as shown by elevated threshold in case reports of ischemia and edema involving the medial part of the Heschl's gyrus and sparing the associative components of the auditory cortex (Habib et al., 1995; Hattiangadi et al., 2005). Congruent with this association, pitch-change detection abilities remained similar to controls in patients with temporal lobe excisions that encroached the superior temporal gyrus while sparing the Heschl's gyrus (Johnsrude et al., 2000).

These findings are corroborated by neuroimaging work showing that the ability to detect pitch-change is related to isolated primary area activations (Griffiths, 2003). By contrast, detection of change in pitch patterns is instead associated with auditory association regions, as shown by additional activations in associative areas located within the superior temporal gyrus (Patterson et al., 2002), the planum temporale (Griffiths et al., 1998; Stewart et al., 2008) or both (Warren and Griffiths, 2003) when participants are exposed to pitch change in a melody. Taken together, these findings suggest that early auditory regions are able to detect if pitch features are same or different between two tones but are unable to detect when this change occurs within a higher-order pattern of at least 3 tones. Mechanistically, therefore, pitch-pattern detection could be acknowledged as a higher order computational early auditory process than pitch-change detection, requiring additional sequential analysis within auditory association regions.

To date, deficits in auditory sensory processing have been extensively described in SZ using both behavioral tone-matching-type paradigms (Donde et al., 2017), as well as neurophysiological paradigms such as mismatch negativity (MMN) that index preattentive auditory change detection within early auditory cortex (Lee et al., 2017; Light and Naatanen, 2013; Naatanen and Kahkonen, 2009). Moreover, low-level auditory deficits such as impaired pitch-change detection correlate with impairments in higher order auditory functions such as prosodic detection or reading (Revheim et al., 2014; Leitman et al., 2005, 2011), suggesting functional consequences. Nevertheless, while several studies have evaluated integrity of pitch-change detection in SZ relative to AER deficits, we are not aware of studies that have similarly investigated integrity of the serial pitch-pattern detection.

To address this gap, we investigated pitch-change and pitch-pattern detection abilities in parallel in SZ, along with integrity of AER as a high-level auditory function. In addition, we evaluated the interrelationship between these measures. Early auditory deficits (e.g. pitch-change and pitch-pattern processing) and higher order deficits (e.g. AER detection) can be viewed as independent deficits each reflecting dysfunction within separate underlying cortical regions. Alternatively, the deficits could be viewed as hierarchically organized, with deficits in low level function propagating sequentially through subsequent levels of processing. To explore these hypotheses, we compared effect sizes and performed a mediation analysis that investigated first, the degree to which pitch-pattern detection was impaired in SZ relative to pitch-change detection, and second, the degree to which pitch-pattern detection mediated the previously reported correlation between pitch-change deficits and higher order auditory function (e.g. AER detection). We predicted that pitch-pattern detection would show similar effect size deficit in SZ to pitch-change detection, but would nevertheless mediate the relationship between pitch-change detection and AER, supporting hierarchical deficits involving early auditory, auditory association and extra-auditory brain parcellations.

2. Method

2.1. Participants

Participants included 27 individuals with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder (SZ) and 40 healthy controls (see Table 1 for demographic information). SZ participants were drawn from a predominant inpatient care setting (Nathan S. Kline Institute, Orangeburg, NY) and controls were recruited from the staff and surrounding community. All participants were screened using the Structured Clinical Interview for DSM-IV (SCID) (Spitzer et al., 1992).

Table 1
Measures across groups. Data are presented as mean (SD).

	SZ ($n = 27$)	Control ($n = 40$)	Cohen's d
Demographics			
Age (years)*	39.3 (10.0)	33.2 (12.3)	
Sex ratio (M/F)**	25/2	25/15	
SES***	25.0 (11.2)	41.6 (10.2)	
Parents' SES*	36.5 (17.7)	45.1 (13.4)	
Lateralization (right/left)	26/1	37/3	
Age first hospitalization	24.1 (8.2)	_	
Illness duration	15.0 (9.9)	_	
CPZ equivalents (mg/d)	724.1 (471.0)	_	
Auditory measures (%correct)			
TMT pitch-change total***	0.70 (0.16)	0.87 (0.11)	$d = 1.15$
Δf 50%***	0.83 (0.16)	0.96 (0.06)	$d = 0.95$
Δf 20%***	0.75 (0.19)	0.93 (0.09)	$d = 1.11$
Δf 10%***	0.68 (0.20)	0.88 (0.14)	$d = 1.13$
Δf 5.0%***	0.65 (0.17)	0.85 (0.17)	$d = 1.06$
Δf 2.5%***	0.58 (0.18)	0.71 (0.17)	$d = 0.89$
TMT pitch-pattern total***	0.58 (0.20)	0.79 (0.14)	$d = 1.21$
Δf 50%**	0.71 (0.24)	0.86 (0.17)	$d = 0.78$
Δf 20%*	0.65 (0.23)	0.80 (0.21)	$d = 0.67$
Δf 10%**	0.58 (0.24)	0.84 (0.18)	$d = 1.18$
Δf 5.0%***	0.50 (0.24)	0.74 (0.22)	$d = 1.00$
Δf 2.5%***	0.44 (0.18)	0.70 (0.18)	$d = 1.48$
Auditory emotion (total)	0.33 (0.06)	0.65 (0.09)	$d = 2.82$
Cognitive and clinical measures			
IQ***	91.4 (12.2)	104.7 (12.3)	
PANSS total	72.2 (12.6)	_	
PANSS positive	19.0 (5.7)	_	
PANSS negative	17.6 (4.8)	_	
PANSS psychopathology	35.7 (6.2)	_	
GAF	44.0 (9.7)	_	
ILS	44.3 (3.5)	_	

CPZ: chlorpromazine; GAF: Global Assessment of Functioning; ILS: Independent Living Scale; IQ: Intellectual Quotient; PANSS: Positive and Negative Syndrome Scale; SES: Socio-Economical Status; TMT = Tone-matching task; Δf = frequency difference.
Missing data: SES (SZ $N = 1$); GAF ($N = 1$); ILS ($N = 2$); IQ (SZ $N = 1$).
* $p < 0.05$.
** $p < 0.005$.
*** $p < 0.0005$.

All participants denied a history of neurological disorders, head injury with loss of consciousness, and current substance abuse/dependence. Controls participants were free of a current DSM disorder and had no lifetime history of schizophrenia-spectrum disorder.

All participants performed a quick-IQ test (Ammons and Ammons, 1962). Clinical assessments included ratings on the Positive and Negative Syndrome Scale (PANSS) (Kay and Sevy, 1990), the problem solving factor of the Independent Living Scale (Revheim and Medalia, 2004; Revheim et al., 2006) and the Global Assessment of Functioning (Aas, 2011). The study was approved by the Institutional Review Board at the Nathan S. Kline Institute. All participants provided written, informed consent, and were paid for their participation.

2.2. Measures

2.2.1. Pitch-change detection task

Pitch-change detection was assessed using a tone-matching task, as described previously (Leitman et al., 2010a, 2010b; Strous et al., 1995). Briefly, this task presents subjects pairs of 100-ms pure tones in series, with 500-ms intertone interval. Within each pair, tones are either identical or differ by predetermined frequencies differences (Δ2.5%, Δ5%, Δ10%, Δ20%, or Δ50%). Tones are derived from 3 reference frequencies (500, 1000, and 2000 Hz) to avoid learning effects. For each pair, participants were asked to listen to tones and report verbally to the tester if the tones were identical ("same") or different ("different"). The test took approximately 20 min to complete. Stimuli were presented through headphones at a comfortable listening level. Participant performance across the 5Δ levels was averaged and this score was used for analysis.

2.2.2. Pitch-pattern detection task

The same set of stimuli were used, but this task presented participants a series of 3 consecutive tones. Within each trio, tones are either all identical or only 1 tone's frequency differs from the others'. For each trio, participants were asked to listen to tones and report verbally if the tones were all identical ("same"), if "1st tone was different, "2nd tone was different", or "3rd tone was different". As with the pitch-change detection, task, performance was averaged across the 5 difficulty levels.

2.2.3. Auditory Emotion Recognition (AER)

AER was assessed using an emotional prosody task as described previously (Leitman et al., 2010a, 2010b). This task consists of 32 sentences recorded from native English speakers conveying 5 emotions (happy, sad, angry, fear or disgust) – or no emotion. The sentences were semantically neutral and consisted of both statements and questions (i.e., "Is it eleven o'clock?", "It is eleven o'clock"). Percent of correctly categorized sentences for each emotion and total were used for analysis.

2.3. Analyses

All statistical analyses were carried out using R version 3 (R Development Core Team, 2008). For all tests, significance was set at *p*-value < 0.05.

Socio-demographic characteristics between groups were compared using independent-sample two-sided Student *t*-tests for continuous values and exact Fisher's exact F for categorical values.

To compare basic auditory processing between groups we used a two-way ANOVA with group (control and patient) as inter-subject factor and task (pitch-change/pitch-pattern detection) as within-subjects factor, followed, in case of significance, by one-way ANOVAs and mean comparison tests (t Student if Gaussian values and U Mann-Whitney if categorical values). Cohen's *d* effect sizes for mean comparisons were calculated with a *d* value of 0.2, 0.5 and 0.8 reflecting the cut-off for small, medium and large effect sizes, respectively (Cohen, 1988).

To inform the further mediation analysis, the relationships between the three main outcomes (pitch-change, pitch-pattern and AER) were determined by Pearson correlations. A multivariate regression analysis was additionally performed to investigate the impact of socio-demographic variables on these three measures (i.e. age, sex, IQ measures and chlorpromazine equivalent) in the SZ group.

We employed the structural equation modeling function (SEM) of the Latent Variable Analysis LAVAAN 23.1 package (Rosseel, 2012) to conduct the mediation analysis using path diagram coefficient. Mediation analysis is more informative than simple multivariate regression since it allows to consider an additional type of variable, called a mediator, which can help determine how an independent variable influences a dependent variable. Hence, mediation analysis is more relevant to test for a hypothesized causal and temporally ordered sequence between at least three different measures (Baron and Kenny, 1986; Mackinnon and Fairchild, 2009).

Based on our hypothesis and on the correlation analysis, we planned to use a three-variable mediation model to establish if the mediator variable (here, pitch-pattern detection) fully mediates a relationship between the dependant (AER performances) and an independent variable (pitch-change detection) in the SZ group by estimating the effect of the dependant variable on the independent variable controlling for the mediation variable (Preacher and Hayes, 2008). If that is the case, this effect should not be significant. Effects between variables were estimated as path diagram coefficients ('*path*'), which can be conceptualized as regression coefficients that measure an association between two variables (Gelfand et al., 2009).

3. Results

3.1. Auditory tonal processing tasks and emotion recognition

Results of the tonal processing and AER tasks are shown in Fig. 1. The two-way ANOVA revealed a significant main effect of group ($F_{(1,133)} = 50.93$, $p < 0.0001$) and task ($F_{(1,133)} = 14.25$, $p = 0.0002$) across the pitch-change and pitch-pattern detection tasks but no significant group by task interaction ($F_{(1,133)} = 0.60$, $p = 0.44$). Both controls and patients showed better performance in the pitch-change than pitch-pattern detection task (both $p < 0.01$). Nevertheless, the magnitude of the deficits in SZ participants was similar and large in the pitch-change ($d = 1.15$) and pitch-pattern ($d = 1.21$) tasks. Performance on the AER task was also significantly reduced in SZ patients vs. representative controls, with extremely large effect size ($d = 2.82$).

Additional univariate regression analyses were conducted for each of the three tasks with age, gender, SES, parents' SES and IQ as covariates, since these socio-demographic characteristics significantly differed between groups and may impact in auditory processing abilities. The effect of group remained significant for all tasks (all p's < 0.05).

3.2. Relationships among auditory measures

In the SZ group, performance in both the pitch-change ($n = 27$; $r = 0.48$, $p = 0.01$) and pitch-pattern ($n = 27$; $r = 0.59$, $p = 0.001$) tasks correlated significantly with impaired AER performance, but these correlations lost significance within the control group and across groups (all p's > 0.05). Additionally, pitch-change and pitch-pattern tasks performances were significantly correlated with each other both within and across groups (partial $r = 0.81$, $p < 0.0001$). Multiple linear regressions performed in the SZ group including age, sex, IQ measures and chlorpromazine equivalent showed a significant association between AER and pitch-pattern detection only ($R^2 = 0.33$, $F_{(6,19)} = 5.88$, $p = 0.025$).

3.3. Mediation analysis

Mediation analysis evaluated the relationship between pitch-change detection, pitch-pattern detection and AER performance in the

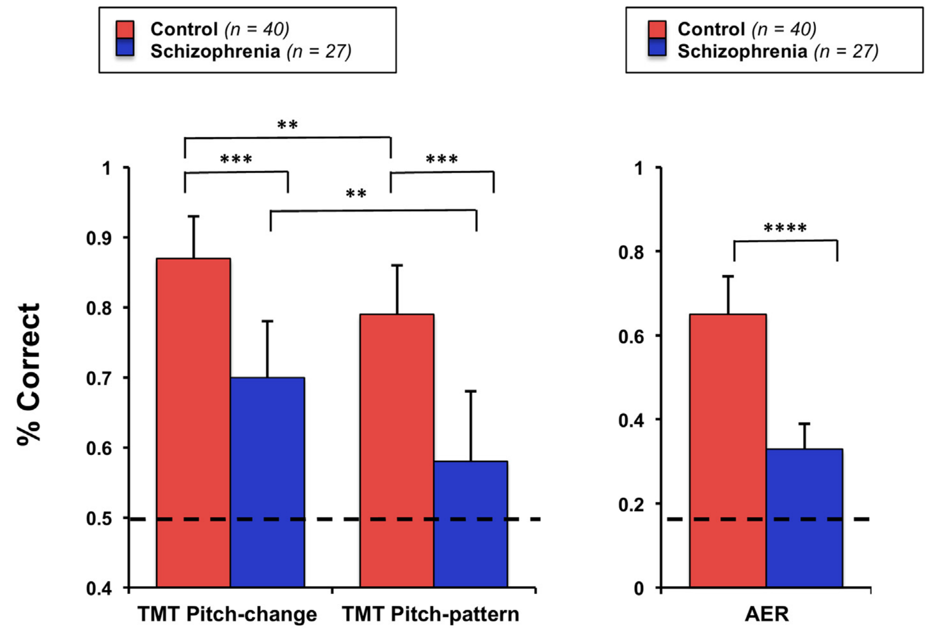

Fig. 1. Behavioral assessment of tone-matching (TMT) and auditory emotion recognition (AER) tasks. **** = $p < 0.0001$, *** = $p < 0.001$, ** = $p < 0.01$ Chance performances for TMT pitch-change (2 choices), TMT pitch-pattern (4 choices) and AER (6 choices) are indicated by a dash-line.

SZ group. For this analysis, the pitch-change detection total percent correct was entered as the independent variable and the pitch-pattern detection total percent correct as the mediator variable. AER total percent correct was entered as the dependent variable.

As shown in Fig. 2, *path a* estimates the effect of pitch-change detection on pitch-pattern detection, *path b* the effect of pitch-pattern detection on AER and *path c* the effect of pitch-change detection on AER. The analysis showed that pitch-change detection had a highly significant total effect on AER along with a significant indirect effect. The direct effect of pitch-change detection on AER did not reach significance, suggesting that pitch-change detection effect on AER can be mediated by pitch-pattern detection. However, larger effect size of total effect shows that pitch-change detection is also involved in AER regardless of pitch-pattern detection abilities.

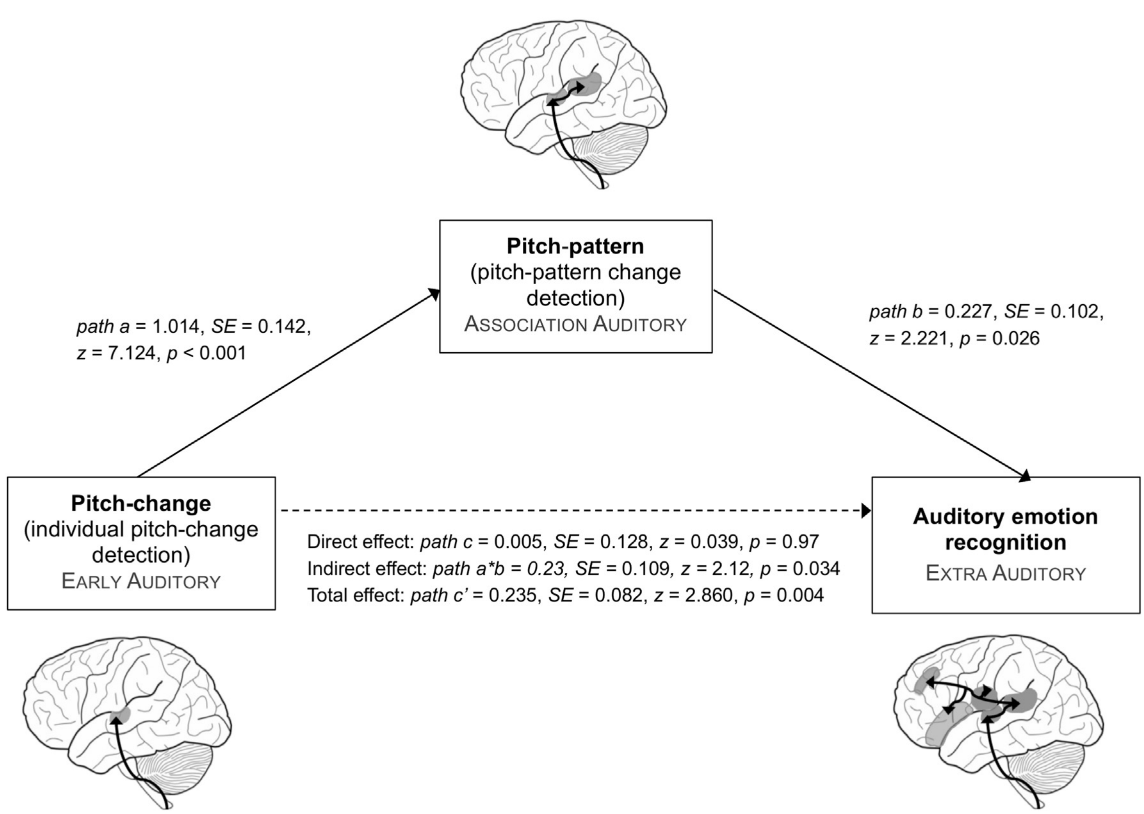

Fig. 2. Mediation model for patients with schizophrenia between pitch-change detection, pitch-pattern detection and auditory emotion recognition. Potential brain structures and steps of the auditory pathway corresponding to the behavioral measures are represented. Arrows = pathway of the auditory stimulus, grey = corresponding brain structures. Extra auditory structures = insula, limbic system, cingular cortex, inferior frontal gyrus.

4. Discussion

4.1. Hierarchical tonal processing deficits

The primary finding of the present study is that patients with SZ show profound deficits in tonal processing ability based upon both pitch-change and pitch-pattern discrimination. Pitch change-detection deficits in SZ have been widely reported in the literature and have previously been shown to correlate with impaired AER (review in Donde et al., 2017), while the relationship between pitch-pattern detection and AER has not been previously examined. Assuming that pitch-change detection and pitch-pattern detection localize to early-auditory and auditory-association parcellations respectively, the absence of condition effect in the repeated-measures analysis involving the two auditory measures support the hypotheses, first, that deficits are observed even in additional phases of early processing and, second, that no additional deficit is observed in auditory association vs. early auditory regions.

These finding are consistent with several studies involving different clinical pictures across the psychotic continuum that show a global grey matter loss encompassing all areas of the auditory cortices in at-risk (Bhojraj et al., 2011; McKechanie et al., 2016), first-episode (Kubicki et al., 2002; McCarley et al., 2002) and established SZ (Fusar-Poli et al., 2011) patients. However, more recent findings highlight an abnormal brain-wide connectivity centered at the left Heschl's gyrus (A1) in ultra high-risk subjects (Colibazzi et al., 2017) and a lower isolated Heschl's cortical thickness that correlated with AVH severity in first-episode patients (Chen et al., 2015).

Specifically, neurodevelopmental studies in children indicate that pitch-change detection become adult-like in children aged 6 to 7 years, while the sensitivity to change in pitch-patterns significantly improves later, from 8 to 9 years of age, suggesting that early auditory inputs to the surrounding auditory association structures allowing pitch-pattern detection are crucial over the course of brain development (Trehub et al., 1986; Cooper, 1994; Fancourt et al., 2013). Thus, either early developmental alterations (Rapoport et al., 2012) or neurodegenerative processes during later adolescence described in SZ could account for present findings (Insel, 2010).

4.2. Relationship to higher-order auditory processing impairment

Another significant finding of our study is that both tone-matching conditions, which correlate, also correlate with AER in SZ individuals. This replicates previous work on affective prosody in SZ (Kantrowitz et al., 2015; Gold et al., 2012; Leitman et al., 2005), while correlation between AER and pitch-change detection performances did not reach significance in the study of Jahshan et al., 2013. Consistent with our results, AER deficits in similar tasks have been repeatedly documented in SZ (Kantrowitz et al., 2014, 2015; Jahshan et al., 2013; Gold et al., 2012; Leitman et al. 2005, 2007, 2011).

Here, we provide the original findings that first pitch-pattern detection correlates significantly with AER and also appears to mediate the previously reported relationship between pitch-change detection and AER in patients. In addition, our mediation analysis suggests that besides detection of pitch-change contributing to detection of pitch-pattern, pitch-change detection is important on its own in decoding auditory emotion. These findings are consistent with the crucial role of pitch variability (e.g., standard deviation of fundamental frequency) and proportion of spectral energy ratios for emotion categorization (Juslin and Laukka, 2001; Leitman et al., 2008; Kantrowitz et al., 2013)

Mechanistically, in addition to involvement of early auditory and auditory association regions, AER deficits in patients have been related to temporal connectivity and activation impairments of further regions such as the frontal gyri, structures of the limbic system (Leitman et al., 2007, 2010a, 2010b, 2011) and the insula (Kantrowitz et al., 2015). This suggests a comprehensive pathway of auditory emotion brain mechanisms where pure sounds are first processed at the level of early auditory cortex, then auditory association and finally multisensory structures. In patients, the deficit would occur at the early stage of A1 processing which would then disrupt the inputs to subsequent areas of the pathway.

Whereas the effect sizes for pitch-change detection and pitch-pattern detection were similar ($d = 1.15$ and $d = 1.21$, respectively) the magnitude of deficit in AER was much larger ($d = 2.82$). Thus, while limited additional pathology appears to be present between early auditory cortex and auditory association regions, significant additional dysfunction appears to occur within wider auditory emotion recognition networks, potentially involving both posterior (e.g. pSTS) and anterior (e.g. insula, medial prefrontal cortex) brain regions. Many of these regions have undergone extensive expansion during primate evolution, are late-developing in humans, and thus may be particularly susceptible to neurodegeneration (Hill et al., 2010).

4.3. Limitations

Despite the original findings, there are specific limitations to the present study. First, it is possible that participants with SZ may perform more poorly on the tone-matching tasks due to increased attentional lapses, a prevalent cognitive impairment in SZ (Fioravanti et al., 2012). However, we have previously shown that once adjustment is made for sensitivity deficits, patients have no more sensitivity than controls to a variety of attention-related paradigmatic manipulations, including introduction of a delay (Javitt et al., 1997), cross modality distractor (Javitt et al., 1997) or within-modality distractor (Rabinowicz et al., 2000). Thus, the deficit is more likely to reflect imprecision of the auditory representation rather than increased distractibility (Javitt and Sweet, 2015).

Second, compared to pitch-change, pitch-pattern stimuli can be viewed as an increase in the sensory load thus engaging higher order auditory process such as working memory. However, it has been described that 3 or more sequential notes are automatically treated as a unitary item (“melody”) (Cook et al., 2004; Piazza et al., 2013). For example, if a tonal pattern sequence is interrupted by a deviant triad, an MMN results even though the note that disrupts the pattern is not a deviant relative to prior individual notes in the sequence (Alain et al., 1999; Haigh et al., 2017). Thus, the critical structures for pitch-pattern discrimination are those that relate to melodic processing within auditory cortex (as discussed by Griffiths, 2001, 2003) rather than more abstract concepts of “load”.

Third, it is possible that auditory information can bypass early auditory cortex via ascending pathways from several structures located in the thalamus to auditory association regions. These pathways are well-documented in non-human primates (Pandya et al., 1994; Hashikawa et al., 1995; Hackett et al., 1998). Thus, similar magnitude deficits in early auditory and auditory association regions may reflect parallel impairments in subcortical as well as cortico-cortical information processing.

Fourth, all patients were receiving antipsychotic medication, so that medication effects on tonal processing and AER abilities cannot be excluded. Nevertheless, tone-matching scores did not correlate with medication dose and correlations between both tone-matching conditions and AER remained significant even following covariation for dose.

Finally, while AER depends heavily on discrimination of pitch-changes, it also integrates other types of information (e.g. intensity, timbre) that were not tested here. Such processes are also decoded at the level of early auditory and auditory association cortex, are also reported to be abnormal in SZ (Leitman et al., 2010a, 2010b) and may contribute to AER deficits in patients.

5. Conclusion

Deficits in pitch-change detection are well-replicated in SZ. By contrast, integrity of pitch-pattern detection abilities has not been previously examined. Moreover, this process is more proximate to prosodic detection in SZ than individual pitch-change detection, and maps primarily to association regions of auditory cortex that are known to project to emotion-related brain regions. We show deficits in pitch-change and pitch-pattern detection that are similar in effect size, suggesting primary pathology at or before early auditory cortex. Consistent with hierarchical models, effects of pitch-change deficits on AER were mediated indirectly through pitch-pattern detection.

These findings suggest that investigations of pitch-pattern detection may be useful in assessing auditory sensory dysfunction in SZ along with pitch-change, and that convergent impairments in input to higher order association regions, as well as intrinsic dysfunction or dysconnectivity of those regions, may contribute to higher order cortical dysfunction.

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