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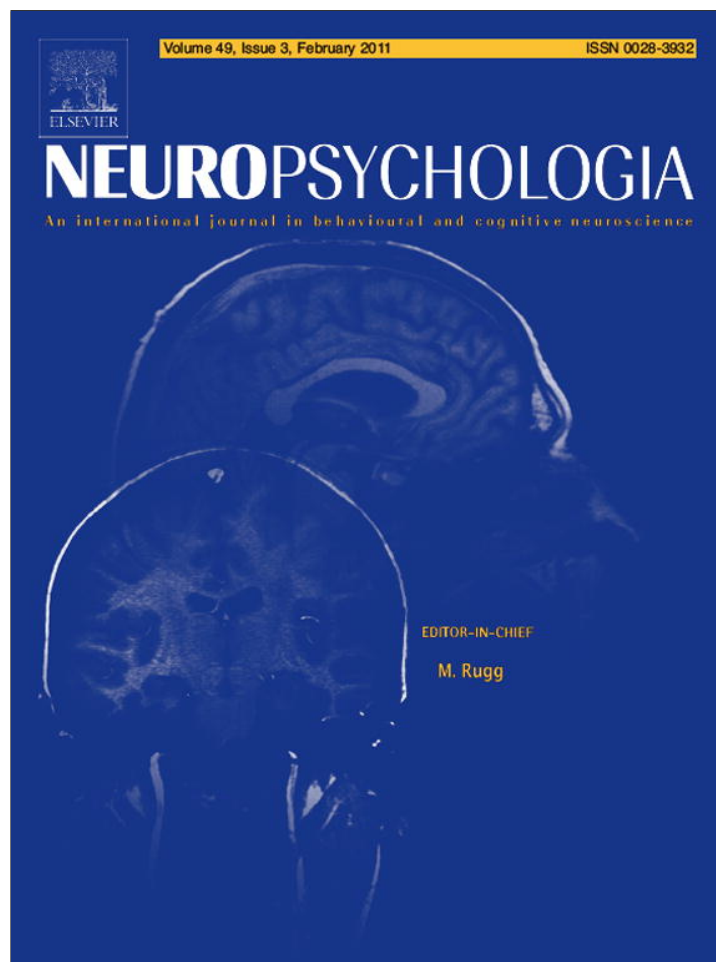
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Atypical processing of auditory temporal complexity in autistics

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ABSTRACT

Autistics exhibit a contrasting combination of auditory behavior, with enhanced pitch processing abilities often coexisting with reduced orienting towards complex speech sounds. Based on an analogous dissociation observed in vision, we expected that autistics' auditory behavior with respect to complex sound processing may result from atypical activity in non-primary auditory cortex. We employed fMRI to explore the neural basis of complex non-social sound processing in 15 autistic and 13 non-autistics, using a factorial design in which auditory stimuli varied in spectral and temporal complexity. Spectral complexity was modulated by varying the harmonic content, whereas temporal complexity was modulated by varying frequency modulation depth. The detection task was performed similarly by autistics and non-autistics. In both groups, increasing spectral or temporal complexity was associated with activity increases in primary (Heschl's gyrus) and non-primary (anterolateral and posterior superior temporal gyrus) auditory cortex. Activity was right-lateralized for spectral and left-lateralized for temporal complexity. Increasing temporal complexity was associated with greater activity in anterolateral superior temporal gyrus in non-autistics and greater effects in Heschl's gyrus in autistics. While we observed similar hierarchical functional organization for auditory processing in both groups, autistics exhibited diminished activity in non-primary auditory cortex and increased activity in primary auditory cortex in response to the presentation of temporally, but not of spectrally complex sounds. Greater temporal complexity effects in regions sensitive to acoustic features and reduced temporal complexity effects in regions sensitive to more abstract sound features could represent a greater focus towards perceptual aspects of speech sounds in autism.

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1. Introduction

Behavioral evidence indicates that the cognitive architecture of visual and auditory perceptual processing may be differently organized in autism (Behrmann, Thomas, & Humphreys, 2006; Dakin & Frith, 2005; Mottron, Dawson, Soulières, Hubert, & Burack, 2006; Samson, Mottron, Jemel, Belin, & Ciocca, 2006). The diagnostic criteria for autism (Lord et al., 1997) include signs related to both hypo- and hyper-reactivity to sounds (Grandin & Scariano, 1986; Metz, 1967; Novick, Vaughan, Kurtzberg, & Simson, 1980). While autistics¹ may display apparent disinterest in speech sounds, and

aversive reactions to vacuum cleaner and crowd noises (Goldfarb, 1961), they may also have heightened musical interests, and enhanced auditory abilities such as superior pitch memory and pure tone discrimination (Bonnell et al., 2003; Heaton, 2003).

Auditory processing atypicalities in autism have been interpreted in two frameworks. Weak central coherence theory (Frith & Happe, 1994) hypothesizes that autistics have difficulty integrating local auditory features into larger ensembles at the global level (Kellerman, Fan, & Gorman, 2005; Nieto Del Rincon, 2008). However, reports of intact global auditory processing in autism challenge this hypothesis (Heaton, 2005; Mottron, Peretz, Belleville, & Rouleau, 1999; Mottron, Peretz, & Menard, 2000). The enhanced perceptual functioning model (EPF) (Mottron et al., 2006) describes both the superiorities of processing local features and the intact global contour processing within hierarchical auditory patterns (e.g. melody). Moreover, this model emphasizes the link between the bias towards local elements in hierarchical auditory patterns and superior pitch detection for pure tones

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¹ The term "autistic" rather than "person with autism" is used in a respectful manner (see Sinclair, 1999).

(Heaton, 2003; Mottron et al., 2000). However, the EPF predictions regarding the processing of psychophysically complex sounds are essentially derived from evidence reported from studies investigating early visual processing that have demonstrated superior abilities in autistics for simple, luminance-defined, information extracted by mechanisms operating within primary (V1) visual cortex (Bertone, Mottron, Jelenic, & Faubert, 2005; Plaisted, O'Riordan, & Baron-Cohen, 1998), and lower performance for tasks involving more complex visual processing requiring involvement of both primary (V1) and non-primary (V2, V3) regions of visual cortex (Bertone, Mottron, Jelenic, & Faubert, 2003; Bertone et al., 2005; Blake, Turner, Smoski, Pozdol, & Stone, 2003; Milne et al., 2002; Pellicano, Gibson, Maybery, Durkin, & Badcock, 2005; Vandembroucke, Scholte, van Engeland, Lamme, & Kemner, 2009). Atypical integration between primary and non-primary regions of the visual cortex could underlie this dissociation (Bertone et al., 2005). This heuristic was recently extended to audition, resulting in predictions of differential processing by autistics for simple, compared to complex, auditory stimuli (Samson et al., 2006). In support of this idea, enhanced pitch processing has been documented in numerous behavioral (Bonnell et al., 2010, 2003; Heaton, 2003, 2005; Jones et al., 2009; O'Riordan & Passetti, 2006) and electrophysiological studies of autistics (Ferri et al., 2003; Gomot, Giard, Adrien, Barthelemy, & Bruneau, 2002; Lepisto et al., 2008, 2005). In some cases, the behavioral advantage reaches outstanding levels, extending beyond four and five standard deviations above the mean of the control group (Heaton, Davis, & Happe, 2008). Moreover, superior processing of individual sound components might underlie enhanced chord disembodiment (Heaton, 2003; Miller, 1989; Mottron et al., 1999) or the unimpaired discrimination of non-social complex sounds in autistics if they were to achieve successful processing through the decomposition of complex sounds (Bonnell et al., 2010).

The relevance of studying auditory perception in autism is not limited to the peaks of ability, as most studies report diminished abilities in processing social auditory information in this population. This is the case for speech recognition in noise (Alcantara, Weisblatt, Moore, & Bolton, 2004; Groen et al., 2009) or prosody perception (Kujala, Lepisto, Nieminen-von Wendt, Naatanen, & Naatanen, 2005; Peppe, McCann, Gibbon, O'Hare, & Rutherford, 2007). However, typical voice processing abilities in autistics have been reported (Boucher, Lewis, & Collis, 2000). Event-related potential studies have shown reduced cortical responses to complex speech-like sounds, including vowels (Ceponiene et al., 2003; Lepisto et al., 2005, 2006; Whitehouse & Bishop, 2008) and consonant–vowel syllables (Jansson-Verkasalo et al., 2003; Russo, Zecker, Trommer, Chen, & Kraus, 2009). Finally, reduced activation of the “voice area” in the superior temporal sulcus (STS) has been reported in autistic adults (Gervais et al., 2004), and a reduced leftward asymmetry has been observed for speech processing (Boddaert et al., 2003, 2004; Lepisto et al., 2005, 2006; Minagawa-Kawai et al., 2009). It is therefore plausible that atypical processing of psychophysical properties of complex sounds plays a role in the apparent disinterest for speech, evident in most autistics, at least in their early years.

As in the visual system (Grill-Spector & Malach, 2004), auditory cortical analysis is organized hierarchically, with simple feature extraction at the primary level providing input to non-primary fields that subsequently extract more complex features. This functional organization scheme receives empirical support from both animal and human studies. In non-human primates and cats, the primary or ‘core’ auditory region, located in Heschl's gyrus (HG), is more tonotopically organized by frequency, has sharper frequency tuning and shows lower thresholds to pure tones as compared to non-primary auditory fields (Merzenich & Brugge, 1973; Morel, Garraghty, & Kaas, 1993; Rauschecker, Tian, & Hauser,

1995; Schreiner & Cynader, 1984). The non-primary neurons within the superior temporal gyrus (STG), labeled as ‘belt’ and ‘parabelt’ auditory regions, show broader individual frequency tuning, collectively respond to a broader range of frequencies and are selectively responsive to more complex stimuli such as band-passed noise (Rauschecker et al., 1995; Recanzone, 2000). These physiological findings combined with the known anatomical connections among primary and associative auditory regions (Hackett, Stepniewska, & Kaas, 1998) lend support to hierarchical organizational accounts of information flow in non-human auditory cortex (Kaas & Hackett, 1998, 2000; Rauschecker, 1998). Similar organizational plans are evident in human auditory cortex. An fMRI study reported that pure tone presentation resulted in activity increases in primary auditory cortex (HG), whereas complex band-passed noise elicited activity increases extending to the surrounding non-primary auditory fields in the anterolateral aspect of HG and STG (Wessinger et al., 2001), consistent with the location of the belt region in macaques (Rauschecker, 1998). Similarly, imaging studies have consistently revealed that *spectrally* complex sounds, with multiple harmonic components, and *temporally* complex sounds, with varying frequency or amplitude in time, elicit activity increases extending to non-primary auditory areas in anterior, lateral and posterior STG, corresponding to the belt and parabelt regions (Binder et al., 2000; Giraud et al., 2000; Hall et al., 2002; Hart, Palmer, & Hall, 2003; Schonwiesner, Rubsamen, & von Cramon, 2005a; Schonwiesner & Zatorre, 2009; Thivard, Belin, Zilbovicius, Poline, & Samson, 2000; Zatorre & Belin, 2001). Moreover, while primary areas (HG) are sensitive to acoustic variations in speech sounds, non-primary areas within anterior and posterior superior temporal regions are more responsive to abstract sound features like intelligibility than to acoustic signal variations (Okada et al., 2010), supporting the role of these non-primary fields in the processing of more complex auditory information (Rauschecker & Scott, 2009). In addition to a within-hemisphere hierarchical architecture, auditory processing models also incorporate lateralization features (Zatorre, Belin, & Penhune, 2002) mainly, a leftward asymmetry of the auditory cortical response to temporal sound variation (Belin et al., 1998; Jamison, Watkins, Bishop, & Matthews, 2006; Schonwiesner et al., 2005a; Zaehle, Wustenberg, Meyer, & Jancke, 2004; Zatorre & Belin, 2001) and rightward to spectral sound variation (Jamison et al., 2006; Patterson, Uppenkamp, Johnsrude, & Griffiths, 2002; Schonwiesner, Rubsamen, & von Cramon, 2005b; Zatorre & Belin, 2001).

We used fMRI to examine differential auditory cortical responses to stimuli of varying spectral and temporal complexity in autism. Before being able to account for differential behavioral performances in naturalistic situations, and specifically for atypical autistic performance in music, language and voice processing, a preliminary study exploring the effects of variation in fundamental sound properties is required. For this purpose, we exposed our participants to simple and controlled stimuli, that is pure tones, in addition to spectrally and temporally complex sounds. Although spectral and temporal acoustic features are important characteristics of more complex sounds like speech, it is important to note that the stimuli used here do not represent actual features of speech and remain very simple in comparison to components like vowels, consonants or the structure of formants.

We define sounds as *spectrally complex* when they include more than one frequency component or harmonic. Similar stimuli have been used to investigate cortical auditory spectral complexity processing (Hall et al., 2002; Hart et al., 2003). We define *temporally complex* sounds as having frequency variation over time. Similar frequency-modulated sounds have been used in imaging studies (Hall et al., 2002; Hart et al., 2003). Our experiment is novel in this regard, as we use a parametric design with three levels of temporal complexity with increasing fre-

Table 1

Participant characteristics: Groups were matched on sex, age, IQ, Raven Progressive Matrices percentile scores and manual preference, which is reported as the Edinburgh score with –100 corresponding to completely left-handed and +100 to completely right-handed. ADI is the Autism Diagnostic Interview. Group differences were assessed using independent sample *t*-tests.

	TYP	AUT	<i>p</i>
Sample size (sex)	13 (2 F, 11 M)	15 (2 F, 13 M)	
Age (y:m)			
Mean (SD)	23:6 (7:5)	24:4 (6:3)	0.74
Range	16–39	14–35	
Full-scale IQ			
Mean (SD)	109.6 (10.8)	100.3 (13.9)	0.07
Range	92–131	78–126	
Performance IQ			
Mean (SD)	106.3 (13.0)	100.3 (11.8)	0.22
Range	87–133	86–117	
Verbal IQ			
Mean (SD)	111.1 (10.7)	100.4 (16.4)	0.06
Range	93–127	72–121	
Raven			
Mean (SD)	72.3 (23.2)	70.4 (31.5)	0.86
Range	19–98	6–100	
Handedness			
Mean (SD)	+61.2 (41.1)	+71.9 (49.0)	0.62
Range	–45 to +100	–100 to +100	
ADI score mean (cut-off)			
Social		24.1 (10)	
Communication		18.2 (8)	
Behavior		7.0 (3)	
ADI score mean (cut-off)			
Social		11.0 (6)	
Communication		6.0 (3)	
Behavior		16.7 (10)	

quency modulation depth while maintaining constant modulation rate.

On the basis of previous work in typical individuals, we predicted that sounds of higher spectral and temporal complexity would induce increased activity in primary (HG) and non-primary auditory cortex, mainly with spatial extension to anterolateral STG (Hall et al., 2002; Hart et al., 2003). Based on hypothesized reduced integration among auditory cortical regions (Bertone et al., 2005; Samson et al., 2006), autistics should exhibit reduced activity in response to complex auditory material in non-primary auditory areas, with higher sensitivity to complex sound features. Between-group effects would possibly be more important in response to temporal complexity, which is specifically important for speech recognition, particularly low modulation rates as the one used here (Houtgast & Steeneken, 1985; Tallal, Miller, & Fitch, 1993). In terms of response lateralization, we expected a rightward asymmetry associated with spectral complexity and leftward for temporal complexity.

2. Material and methods

2.1. Participants

Thirteen typical (TYP) and 15 autistic (AUT) participants were included in this study. There were no significant differences in mean chronological age, Wechsler IQ scored with Canadian Norms (Wechsler, 1991; Wechsler, 1997), Raven's Progressive Matrices scored with norms for North America (Burke, 1985) or manual preference (Table 1). All but one participant in each group were right-handed. All had normal hearing as measured by pure-tone audiometry and no formal musical training. TYP participants were screened for any personal or familial neurological or medical conditions known to affect brain function. One AUT participant was medicated (lorazepam) at the time of testing. Informed written consent was obtained from all participants, and from the parents for minors, in accordance with the Regroupement Neuroimagerie Québec IRB approved protocol #2006-0204. All participants were compensated.

All participants were recruited from the database of the Pervasive Developmental Disorders specialized clinic of the Rivière-des-Prairies Hospital (Montréal, Canada). Exclusion criteria included a personal or family history of psychiatric or neurological disorders other than autism. The AUT participants were character-

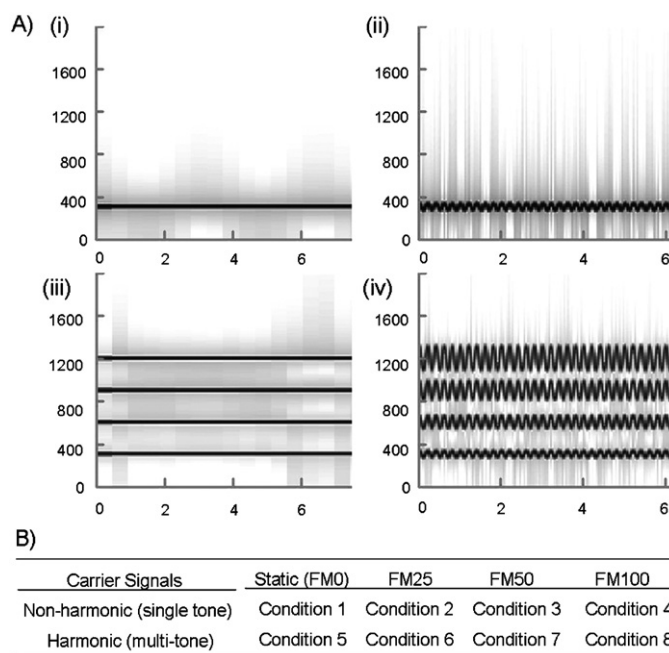


Fig. 1. The auditory stimuli were varied in both spectral and temporal complexity. (A) Spectrogram (decomposition of acoustic energy along time and frequency) of the stimuli. Frequency is shown in the vertical axis and time is represented in the horizontal axis. The energy level is represented by the greyscale (white (0) – black (96) dB). The four extreme conditions are represented here: (i) Unmodulated pure tone (condition 1), (ii) 100% modulated pure tone (condition 4), (iii) Unmodulated harmonic tone (condition 5) and (iv) 100% modulated harmonic tone (condition 8). (B) Table of the 8 conditions.

ized using a combination of standard instruments including the Autism Diagnostic Interview Revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994), the Autistic Diagnostic Observation Schedule (ADOS-G module 3 or 4) (Lord et al., 1989) and clinical evaluation based on DSM-IV criteria.

2.2. Stimuli

The stimuli were synthesized at 44.1 KHz with 16 bit resolution using MITSYIN (Henke, 1976). Sounds were presented continuously for 6.24 s, including a quarter of a sine wave onset and offset ramp (50 ms). Eight stimulus classes were created by crossing two types of carrier signals (single- and multi-tone) with four levels of frequency modulation (FM) (0% (static), 25%, 50%, 100%). The carrier signal was either a 300 Hz pure tone or a harmonic tone with a 300 Hz fundamental and components of equal amplitude at 300, 600, 900, 1200 Hz. The 300 Hz pure tone stimulus was generated using a sine wave oscillator. The harmonically complex tones were generated using a waveform oscillator generating the first four harmonics of a 300 Hz fundamental. A second oscillator was used to modulate the frequency of the carrier oscillator. The frequency of the FM sounds varied at a rate of 5 Hz and the modulation depth differed across FM conditions (0%, 25%, 50% and 100%). Specifically, the depth of modulation defined the limits between which the frequency of the second tone oscillator warbled ($\pm\%$ of FM). For instance, the 300 Hz component varied from 250 to 350 Hz at 100% FM (± 50 Hz), while the warble was (± 12.5 Hz) at 25% and (± 25 Hz) at 50%. We used two spectral (single tone and harmonic) and four temporal (FM0, FM25, FM50, FM100) levels of complexity (Fig. 1). A ninth silence condition was added as a baseline.

2.3. Task

Subjects listened to the stimuli and indicated, by pressing a button, if the sound was modulated or not. This controlled listening task was used to maintain the participants' attention and elicit more reliable activation (Hall et al., 2000). Subjects heard stimuli outside the scanner to make certain that they understood the difference between modulated and unmodulated sounds. Stimuli were presented binaurally through MRI-compatible earphones (www.mrconfon.de) at a mean of 85–90 dB sound pressure level (SPL).

On each trial, either one of the eight auditory stimuli or a silence condition was presented. Each run consisted of 72 trials: 64 sound trials (eight for each condition) and eight silence trials, with three runs per subject. The run order was counter-balanced across subjects and trials were presented in pseudo-randomized order within each run using E-Prime 1.1 (Psychology Software Tools). In the fMRI acquisition protocol, each 6.24 s trial occurred prior to image acquisition periods lasting 2.76 s,

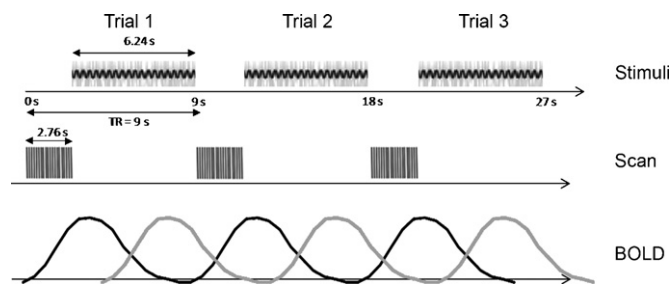


Fig. 2. Stimulus presentation and imaging were interleaved to avoid acoustic noise interference with the task. The stimulus presentation, scan acquisition and hypothetical BOLD-contrast response to scanner noise (black) and to the stimulus (grey) are shown.

using a sparse sampling imaging protocol with an effective TR=9s (Fig. 2). This technique allowed minimizing interference from magnetic gradient noise (Eden, Joseph, Brown, Brown, & Zeffiro, 1999) and improving detection of auditory cortex activity (Belin, Zatorre, Hoge, Evans, & Pike, 1999; Hall et al., 2000).

2.4. Image acquisition

Images were acquired on a 3.0T TRIO MRI system at the “Unité de Neuroimagerie Fonctionnelle” (University of Montreal). The subject’s head was immobilized with foam pads and a vacuum cushion, which helped to stabilize the headphones.

The acquisition began with an anatomical T1-weighted high-resolution image using an MPRAGE sequence (176 slices, voxel size = 1 mm³, 256 mm², TR = 9.7 ms, TE = 4 ms, flip = 12°). Gradient echo phase and magnitude field maps were then acquired (voxel size = 3 mm³, 64 × 64, TR = 300 ms, TE short = 5.71 ms, TE long = 8.17 ms, Flip = 55°) to correct image distortions and improve the coregistration accuracy (Hutton et al., 2002). Echoplanar images were acquired during three 10.8 min runs of 72 scans (TE = 30 ms, voxel size = 3.4 mm³, 46 slices, flip angle = 90°).

2.5. Behavioral analyses

Group × task ANOVAs examining effects of group, spectral and temporal complexity were carried out on reaction time (RT) and accuracy (ACC) using a critical threshold of $p < 0.01$. Statistical analysis was restricted to the 11 TYP and 13 AUT participants from the fMRI sample for which behavioral data were available.

2.6. Image analyses

SPM5 was used for preprocessing and statistical modeling. Images were realigned, unwrapped, spatially transformed to the ICBM152 (MNI) space (Collins, Neelin, Peters, & Evans, 1994) and spatially smoothed using a 3D Gaussian filtering kernel of 9 mm FWHM.

First level analyses were conducted for each subject, using a design matrix including the eight stimulus conditions, along with six head motion estimates and a constant term included as covariates of no interest. We modeled the task regressors with a finite impulse response function of 2.76 s bin width, selected to match the single volume acquisition time. A high-pass filter cutoff of 128 s was used to remove low-frequency noise. At the second level, the first-level contrasts for each condition contrasted with the silence baseline were entered in a mixed effects model with three factors: Subject (28 levels), Group (2 levels) and Condition (8 levels). Cortical activity peaks were located using a brain atlas (Duvernoy & Cabanis, 1991).

2.6.1. Within-group contrasts

In each group, weighted contrasts ($p_{FWE\ corrected} < 0.05$) across various condition combinations were used to identify areas showing linear effects with respect to complexity. To isolate the effects of spectral complexity, we contrasted the multi-tone (harmonic) conditions to the single tone conditions. For temporal complexity, the linear effect of the four frequency modulation levels was estimated with a parametric contrast. The resulting positive and negative effects reflected the respective increases and decreases in signal associated with increasing temporal complexity.

2.6.2. Conjunctions

To identify the regions exhibiting similar effects among groups, the contrasts computed in the within-group analysis were used to generate multi-group conjunction maps ($p_{FWE\ corrected} < 0.05$). The harmonic vs. single tone contrast for each group was used to compute a conjunction of activity related to spectral complexity. The same procedure was employed to identify common activity increases and decreases related to increasing temporal complexity.

2.6.3. Between-group contrasts

Linear contrasts were used to identify the regions where the task-related activity varied between the groups. Since we had hypotheses concerning sensitivity differences to complex stimuli in cortical auditory areas, we restricted the analyses

by using an inclusive mask of the conjunction of the respective complexity effects in each group. Additionally, we used an uncorrected threshold ($p_{uncorrected} < 0.001$), because of the expected weaker strength of between-group effects. To investigate between-group differences in spectral complexity, we used a mask of the multi-group conjunction of activity related to harmonic multi-tone vs. single-tone conditions. To investigate temporal complexity effects, we used a mask of regions showing linear activity increases associated with increasing temporal complexity across groups.

2.6.4. Between-group comparisons of mean signal change in regions of interest (ROI)

To investigate effects in primary auditory cortex (PAC), we extracted the changes in activity associated with spectral and temporal complexity within selected ROIs in PAC and the inferior frontal gyrus (IFG). The IFG was included as a comparison region given its known role in processing complex auditory features (Joanisse & Gati, 2003; Zaehle, Geiser, Alter, Jancke, & Meyer, 2008). Both ROIs are included to investigate the specificity of the primary auditory response, which could be argued for if the effect is seen only in the PAC, but not in the IFG ROI. The PAC ROI was derived from an independent meta-analysis of pure tone vs. silence contrasts in typical adult samples (Samson, Zeffiro, Toussaint, & Belin, in press). The IFG ROIs were anatomical masks obtained from WFU PickAtlas (Maldjian, Laurienti, Kraft, & Burdette, 2003). Mean signal changes within these ROIs for each of the eight sounds vs. silence contrasts were extracted for each subject using the REX toolbox (<http://web.mit.edu/swg/software.htm>). Linear mixed effect models investigating Group × ROI × Task effects were computed with the subject factor treated as a random effect.

2.6.5. Hemispheric specialization

Laterality indices (LI) were computed with the LI Toolbox (Wilke & Lidzba, 2007) using both voxel count and voxel value as measures. LI were calculated as: $LI = (\sum \text{Left} - \sum \text{Right}) / (\sum \text{Left} + \sum \text{Right})$, yielding values that ranged between left (+1) and right lateralization (−1). Signs of the reported LIs were inverted (−1: left, +1: right) for consistency with the MNI coordinate system. We computed activity asymmetries in STG and IFG using anatomically defined masks taken from the WFUPickAtlas (Maldjian et al., 2003), using a contrast and subject specific adaptive threshold.

3. Results

3.1. Behavior

We observed no group performance differences on the sound modulation detection task (Table S1). A Group × Spectral Complexity (Non-harmonic, Harmonic) ANOVA on RT revealed no main effect of Spectral Complexity ($F(1, 22) = 2.894, p = 0.103$) and no main effect of Group ($F(1, 22) = 1.295, p = 0.267$). Similarly, the Group × Spectral Complexity ANOVA on ACC did not detect significant main effects or interactions ($F < 1$).

Second, a Group × Temporal Complexity (FM0, FM25, FM50, FM100) ANOVA on RT revealed a main effect of Temporal Complexity, $F(3, 66) = 26.887, p < 0.001$, with the RT being on average 35.5% shorter in the FM100 (fastest) conditions than in the FM25 (slowest) conditions. However, there was no main effect of group ($F(1, 22) = 1.295, p = 0.267$). The same ANOVA on ACC revealed a main effect of Temporal Complexity $F(3, 66) = 17.909, p < 0.001$, with, on average, 32.4% less accurate response in the FM25 conditions than in the FM100 conditions (most accurate). There was no main effect of Group for ACC ($F < 1$).

3.2. Imaging

3.2.1. Spectral complexity

3.2.1.1. Within-group contrasts. We found right auditory cortex sensitivity to spectral complexity in both groups (Table 2), with peak activity in the lateral aspect of HG, 4 mm more medially on the x -axis in the AUT group. Fig. 3(i) shows that, using an uncorrected threshold ($p < 0.001$), both groups showed bilateral activity centered on HG that extended along the anterolateral STG, mainly on the right. No groups exhibited negative spectral complexity effects.

3.2.1.2. Conjunction. A conjunction of multi-tone harmonic vs. single tone non-harmonic condition contrasts (Table S2, Fig. S1)

Table 2
Within-group activity associated with auditory complexity. The coordinates are in MNI space. The critical threshold was $t=4.58$, $p < 0.05$ FWE-corrected (d = Cohen's effect size; k = number of voxels).

Region	Left							Right						
	BA	x	y	z	t	d	k	x	y	z	t	d	k	
Higher spectral complexity														
<i>TYP</i>														
Heschl's gyrus	41							60	−8	4	6.07	0.90	96	
<i>AUT</i>														
Heschl's gyrus	41							54	−10	2	4.83	0.72	4	
Negative spectral complexity														
No significant loci														
Increasing Temporal Complexity														
<i>TYP</i>														
<i>Temporal</i>														
Superior temp. gyrus	41/22	−48	−20	8	13.79	2.04	2218	60	−8	4	16.41	2.43	2192	
<i>Frontal</i>														
Middle frontal gyrus	8	−24	28	46	6.24	0.93	257	30	28	48	6.16	0.92	143	
Superior frontal gyrus	9	−14	44	38	5.27	0.78	32							
Precentral gyrus	4							46	−12	38	5.02	0.74	16	
Superior medial gyrus	10							4	54	10	4.89	0.72	35	
<i>Parietal</i>														
Angular gyrus	39	−46	−64	46	4.89	0.72	550	42	−76	38	5.60	0.83	41	
	39	−52	−68	32	5.57	0.83	340	54	−66	26	4.89	0.72	16	
Precuneus	7	−8	−52	66	5.07	0.75	18	10	−58	50	5.00	0.74	30	
<i>Limbic lobe</i>														
Anterior Cingulate	24	−6	36	−10	5.52	0.82	255							
<i>AUT</i>														
<i>Temporal</i>														
Superior temp. gyrus	41/22	−48	−18	6	13.30	1.97	1133	56	−10	2	13.47	2.00	1303	
Middle temp. gyrus	21	−66	−18	−14	4.82	0.71	3							
Decreasing temporal complexity														
<i>TYP</i>														
<i>Frontal</i>														
Inferior frontal gyrus	45	−32	24	−4	5.12	0.76	40	44	22	2	6.60	0.98	389	
Inferior frontal gyrus	44							40	10	26	5.38	0.80	41	
Superior frontal gyrus	6							4	14	52	5.12	0.77	33	
<i>AUT</i>														
<i>Frontal</i>														
Inferior frontal gyrus	45							54	18	24	5.20	0.77	65	

revealed that spectral complexity activity increases common to both groups were centered on HG bilaterally and extended to its lateral portion, mostly on the right.

3.2.1.3. Between-group contrasts. The comparisons revealed no suprathreshold voxels for the TYP > AUT and AUT > TYP contrasts, suggesting that spectral complexity processing did not differ between the groups.

3.2.1.4. Between-group comparisons of mean signal change in ROI. A mixed model of Group × ROI × Spectral level on mean ROI signal change values revealed a trend for a Group × ROI × Task interaction, $t(863) = -1.86$, $p = 0.063$. The bar plots in Fig. 3(ii) show that activity in PAC ROI tends to be greater in the AUT group.

3.2.2. Temporal complexity

3.2.2.1. Within-group contrasts. To investigate activity related to increasing temporal complexity, the parametric effect of modulation depth levels was computed. These analyses (Table 2, Fig. 4(i)) revealed bilateral clusters encompassing HG and surrounding posterior, lateral and anterior portions of the STG with activity peaks in medial HG in both groups. In TYP, this contrast also revealed activity in frontal and parietal lobes.

Signal decreases associated with increasing temporal complexity (Fig. 4(i), Table 2) revealed significant activity decreases in IFG bilateral in the TYP group and on the right only for AUT.

3.2.2.2. Conjunction. Common signal increases related to increasing temporal complexity revealed bilateral activity centered on HG extending towards the STG, mostly in its anterolateral portion

(Table S2). Fig. S2 reveals that the conjunction analysis also identified activity in the left angular gyrus and that the right insula and IFG commonly showed signal decrease.

3.2.2.3. Between-group contrasts. As shown in Fig. 5 (Table 3), the TYP group showed greater signal increase related to increasing temporal complexity in auditory cortex ($p_{unc} < 0.001$). Specifically, the TYP > AUT contrast revealed bilateral effects in posteromedial HG and in anterolateral STG. The reverse contrast (AUT > TYP) showed no significant effects indicating that no areas were more strongly associated with increasing temporal complexity in AUT.

Between-group temporal complexity effects were studied separately for the single tone and harmonic carrier signals (Fig. 5). For the non-harmonic conditions, one region in right anterolateral STG was more sensitive to temporal complexity increases in the TYP group. The same analysis for the harmonic conditions revealed foci in posteromedial HG and anterolateral STG bilaterally. The comparison of between-group (TYP > AUT) changes associated with harmonic vs. single tone signals revealed stronger sensitivity to increasing temporal complexity in the STG ($p = 0.008$ on the right; $p = 0.019$ on the left) and in posteromedial HG ($p = 0.039$ on the right; $p = 0.023$ on the left).

3.2.2.4. Between-group comparisons of mean signal change in ROI. A mixed model of Group × ROI × Temporal levels on mean ROI signal change values revealed a significant Group × ROI × Task interaction, $t(863) = -8.91$, $p < 0.001$. The plots in Fig. 4(ii) show that activity in PAC ROI in greater in the AUT group. This Group × Temporal effect in PAC ROI was confirmed by examining the simple effect, $t(418) = -2.16$, $p = 0.031$.

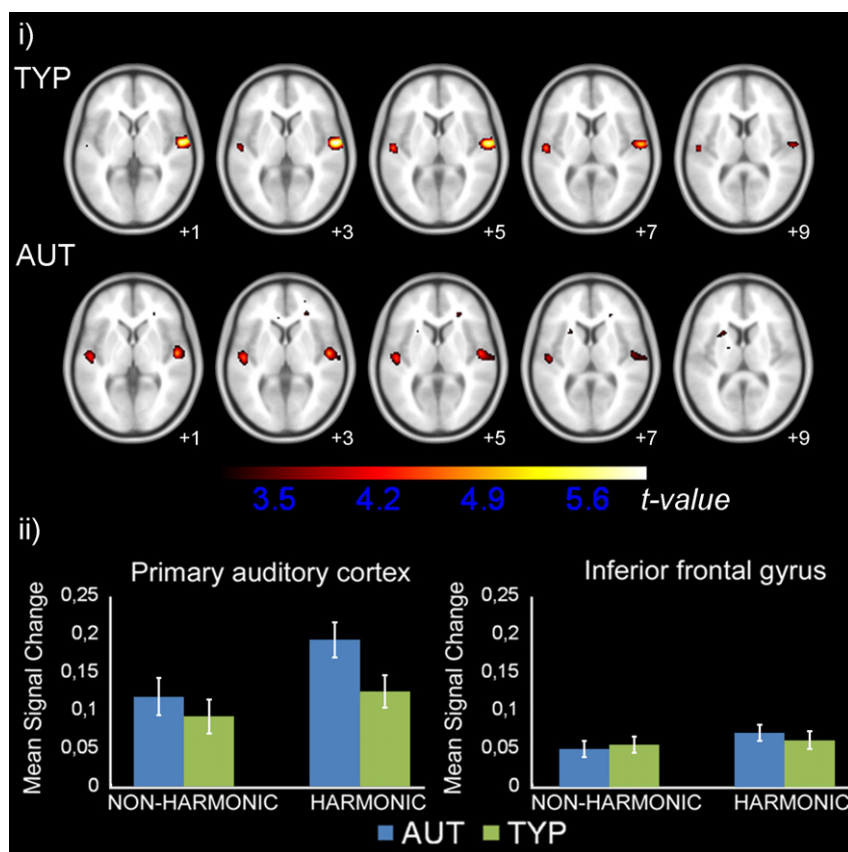


Fig. 3. Spectral complexity is associated with higher activity in primary auditory cortex in AUT. (i) BOLD-contrast activity maps associated with spectral complexity effects in both groups. *T*-statistical maps, using an uncorrected critical threshold of $p < 0.001$, are superimposed on the SPM5 T1 template. Axial images are shown in the neurological convention with MNI *z*-coordinate labels. (ii) Mean signal change in primary auditory cortex (left) and the inferior frontal gyrus (right) for non-harmonic and harmonic conditions. Errors bars represent standard errors.

3.2.2.5. *Hemispheric specialization.* The LI computations (Table S3) for spectral complexity revealed right lateralization for both masks and both groups. Conversely, the LI values computed for temporal complexity revealed left lateralization in both groups for the STG and IFG. No significant between-group differences were observed ($p > 0.05$).

4. Discussion

4.1. Functional organization of auditory complexity processing

The contrast between harmonic and single tone conditions revealed bilateral activity in HG, the location of the primary auditory cortex, with an anterolateral extension of the activity along the STG, mainly on the right. Previous studies comparing harmonic to non-harmonic tones reported either activity in both HG and lateral STG (Hall et al., 2002) or no significant activity (Hart et al., 2003). We report an anterolateral activity extension intermediate between these two studies. Similar patterns have been observed in studies of spectral complexity processing using pure tone sequences varying in frequency, with activity seen in bilateral STG and right STS (Jamison et al., 2006; Zatorre & Belin, 2001) or in right planum temporale (Hyde, Peretz, & Zatorre, 2008). In sum, the present results with respect to spectral modulation are generally in accord with previous imaging studies of non-autistics.

Increasing temporal complexity was associated with bilateral activity clusters centered on HG and extending to postero- and anterolateral STG. Previous studies that used the same 5 Hz modulation rate to compare frequency modulated to unmodulated tones revealed an overlapping pattern (Hall et al., 2002; Hart et al., 2003)

while investigation of frequency modulated speech-like sounds resulted in a comparable pattern (Thivard et al., 2000). Others studies used increasing rates of pure tone alternation within a sequence (Jamison et al., 2006; Zatorre & Belin, 2001) and reported changes limited to HG. Parametric increases in modulation rate of random spectrogram sounds have revealed HG and left anterolateral STG activity (Schonwiesner et al., 2005b), effects also observed for amplitude modulated sounds, albeit with greater response in posterior STG (Giraud et al., 2000; Hart et al., 2003). The convergence between our findings and previous studies indicates that modulation depth is a reliable probe for studying temporal complexity. Lastly, we found similar response lateralization in the two groups: rightward for spectral and leftward for temporal complexity, consistent with previous evidence (Zatorre et al., 2002). In sum, we report a pattern of activity in response to complex vs. simple auditory material demonstrating the hierarchical organization of auditory processing, suggesting that autistics do not differ strongly from controls with respect to this basic architecture. Moreover, the absence of between-group differences and the spatial concordance of activity between groups suggest that the task was performed similarly by all. The task served as an attentional control and was designed for accuracy to be fairly high in all participants; therefore no between-group differences were expected.

4.2. Contribution to current models of auditory processing abilities in autism

On the basis of the visual complexity hypothesis (Bertone et al., 2005), the difference in autistic auditory performance related to

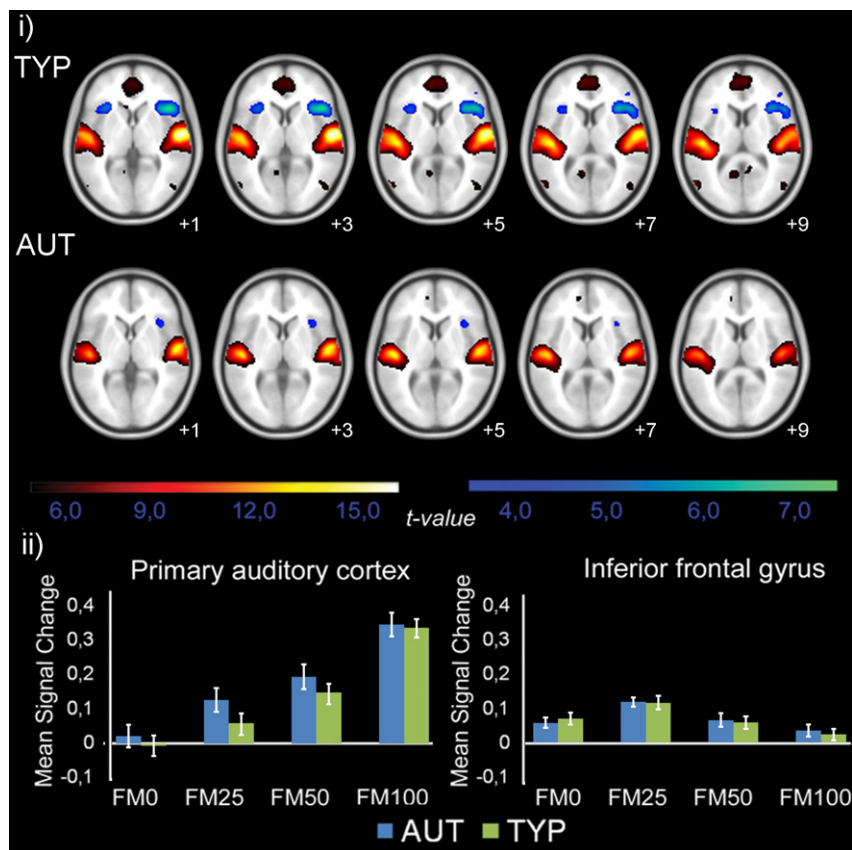


Fig. 4. Increasing temporal complexity is associated with higher activity in primary auditory cortex in AUT. (i) BOLD-contrast activity maps showing temporal complexity effects in both groups. BOLD activity increases (red) and decreases (blue) associated with increasing temporal complexity. *T*-statistical maps, using an uncorrected critical threshold of $p < 0.001$, are superimposed on the SPM5 T1 template. Axial images are shown using the neurological convention with MNI *z*-coordinate labels. (ii) Mean signal change in primary auditory cortex (left) and inferior frontal gyrus (right) for FM0, FM25, FM50 and FM200 conditions. Errors bars represent standard errors.

simple vs. complex processing (Samson et al., 2006), and the hierarchical organization of the auditory system (Wessinger et al., 2001), we expected to observe between-group processing differences in non-primary auditory fields located along the STG. Specifically, autistics should exhibit reduced activity in auditory areas specifically recruited for processing complex auditory stimuli. The current results are consistent with this prediction as autistics showed decreased levels of activity related to temporal complexity in non-primary auditory regions within the STG that are recruited for processing temporally complex sounds in controls (Hall et al., 2002; Hashimoto, Homae, Nakajima, Miyashita, & Sakai, 2000; Talavage, Ledden, Benson, Rosen, & Melcher, 2000).

In contrast, no significant between-group differences related to spectral complexity were seen, supporting the idea that autistics process spectral complexity in a typical fashion. The visual complexity hypothesis suggests that autistics will display reduced non-primary activity related to complex auditory processing. However, this model does not allow predictions specific to the spectral or temporal dimensions. On the other hand, behavioral results largely predict typical spectral complexity processing in autism e.g. intact speech in speech-like noise detection for spectrally but not for temporally modulated noise (Alcantara et al., 2004; Groen et al., 2009), strong musical abilities (e.g. Miller, 1989) and enhanced chord disembodiment (Heaton, 2003; Mottron et al., 1999).

As for temporal complexity, the neural activity differences reported here might be related to specific impaired speech discrimination in temporally modulated noise (Alcantara et al., 2004; Groen et al., 2009). However intact temporally complex non-social

sound processing has also been observed (Bonnell et al., 2010). This indicates that the atypical pattern of activity reported here may be related to unimpaired processing of complex non-social sounds in autism. However, this might not be the case for complex social sound processing. Considering that adequate music perception relies mostly on spectral processing (Warrier & Zatorre, 2002) and that temporal information is crucial for speech recognition (Shannon, Zeng, Kamath, Wygonski, & Ekelid, 1995; Tallal et al., 1993), the dissociation between typical spectral and atypical temporal cortical effects we observed in autistics could explain the dissociation between heightened musical and atypical behavioral and cortical responses related to speech-like or speech sound processing in autistics (e.g. Alcantara et al., 2004; Boddaert et al., 2004; Ceponiene et al., 2003; Lepisto et al., 2005). Although our stimuli were non-linguistic and represent only basic acoustic features, they shared some characteristics of speech such as low frequency modulation rates which are thought to be essential for speech recognition (Houtgast & Steeneken, 1985).

Interestingly, we found stronger between-group differences related to temporal complexity in anterolateral STG for the harmonic compared to the pure carrier signal, when spectral and temporal axes of complexity are combined. This suggests larger between-group effects for more complex auditory material which are expected to elicit more extensive non-primary activity than sounds varying exclusively along spectral or temporal complexity axes (Hall et al., 2002; Hart et al., 2003). This is in line with the visual complexity hypothesis that asserts that differences between groups should emerge for processing information recruiting more extensive neural resources (Bertone et al., 2005).

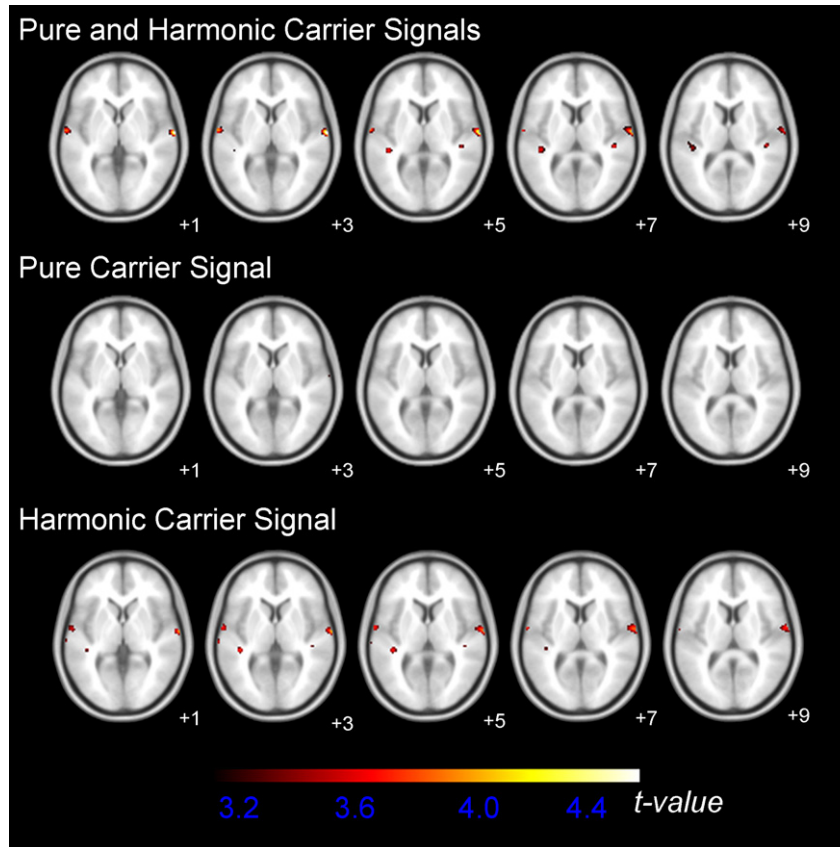


Fig. 5. Activity maps associated with between-group differences in temporal complexity effects. Temporal complexity effects are shown averaged across pure and harmonic carrier signals and separately for pure and harmonic carrier signals. The *t*-statistical map, using an uncorrected critical threshold of $p < 0.001$, is superimposed on the SPM5 T1 template. Axial images are shown using the neurological convention with MNI *z*-coordinate labels.

4.3. Are group differences limited to non-primary regions?

We found greater primary auditory signal change in autistics related to complex auditory processing, more for temporal than

spectral dimensions, indicating that autistics rely more on primary areas, compared to non-autistics, when processing complex sounds. A greater reliance on primary auditory processes in autism could be related to previous demonstrations of greater orienta-

Table 3

Activity associated with group differences in spectral and temporal complexity effects. Temporal complexity is shown for both carrier signals (pure and harmonic tones), pure carrier alone and harmonic carrier alone. The coordinates are in MNI space. The critical threshold was $t = 3.16$, $p < 0.001$ uncorrected (d = Cohen's effect size; k = number of voxels).

Region	Left							Right					
	BA	<i>x</i>	<i>y</i>	<i>z</i>	<i>t</i>	<i>d</i>	<i>k</i>	<i>x</i>	<i>y</i>	<i>z</i>	<i>t</i>	<i>d</i>	<i>k</i>
Spectral complexity													
<i>TYP > AUT</i>													
No significant loci													
<i>AUT > TYP</i>													
No significant loci													
Temporal complexity													
<i>TYP > AUT</i>													
Superior temp. area	22	-64	-8	4	3.93	0.58	47	68	-10	4	4.62	0.69	98
Postero-medial HG	41	-48	-22	14	3.81	0.56	72	46	-26	8	3.76	0.56	23
<i>AUT > TYP</i>													
No significant loci													
Temporal complexity (pure carrier tone)													
<i>TYP > AUT</i>													
Superior temp. area	22							68	-10	4	3.23	0.48	2
<i>AUT > TYP</i>													
No significant loci													
Temporal complexity (harmonic carrier tone)													
<i>TYP > AUT</i>													
Superior temp. area	22	-62	-6	4	3.56	0.53	32	68	-10	4	3.95	0.58	94
		-68	-22	4	3.43	0.51	6						
Postero-medial HG	41	-42	-32	6	3.61	0.53	17	44	-28	6	3.23	0.48	2
<i>AUT > TYP</i>													
No significant loci													

tion towards the low-level, perceptual information in speech (i.e. pitch) in autism (Heaton, Hudry, Ludlow, & Hill, 2008; Jarvinen-Pasley, Wallace, Ramus, Happe, & Heaton, 2008). Moreover, the reduced level of activity in auditory STG regions specifically sensitive to the non-acoustic features of speech stimuli, and increased activity within the HG region, more sensitive to acoustic variations in sounds (Okada et al., 2010), might represent the correlate of a more perceptually based processing style for speech sounds in autism (Heaton, Hudry, et al., 2008; Jarvinen-Pasley et al., 2008). As emphasized by the EPF model (Mottron et al., 2006), analysis within a processing hierarchy is biased towards lower-levels in autism (Soulieres et al., 2009). Furthermore, the EPF model would predict a stronger engagement of primary regions for processing simple tones, as enhanced pitch processing abilities in autism is the most replicated and robust finding related to atypical auditory processing (e.g. Bonnel et al., 2003; Heaton, 2003; Lepisto et al., 2008; O'Riordan & Passetti, 2006). However, our study was insufficiently powered to detect between-group differences in pure tone processing and a direct investigation of this prediction remains to be conducted. The findings of diminished non-primary and increased primary auditory sensitivity for complex sounds suggest that, as in vision (Bertone et al., 2005), complexity is a relevant variable in characterizing auditory processing mechanisms in autism.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuropsychologia.2010.12.033.

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