Speech acquisition predicts regions of enhanced cortical response to auditory stimulation in autism spectrum individuals

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ABSTRACT

A continuum of phenotypes makes up the autism spectrum (AS). In particular, individuals show large differences in language acquisition, ranging from precocious speech to severe speech onset delay. However, the neurological origin of this heterogeneity remains unknown. Here, we sought to determine whether AS individuals differing in speech acquisition show different cortical responses to auditory stimulation and morphometric brain differences. Whole-brain activity following exposure to non-social sounds was investigated. Individuals in the AS were classified according to the presence or absence of Speech Onset Delay (AS-SOD and AS-NoSOD, respectively) and were compared with IQ-matched typically developing individuals (TYP). AS-NoSOD participants displayed greater task-related activity than TYP in the inferior frontal gyrus and peri-auditory middle and superior temporal gyri, which are associated with language processing. Conversely, the AS-SOD group only showed enhanced activity in the vicinity of the auditory cortex. We detected no differences in brain structure between groups. This is the first study to demonstrate the existence of differences in functional brain activity between AS individuals divided according to their pattern of speech development. These findings support the Trigger-threshold-target model and indicate that the occurrence of speech onset delay in AS individuals depends on the location of cortical functional reallocation, which favors perception in AS-SOD and language in AS-NoSOD.

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1. Introduction

Individuals with early socio-communicative abnormalities, repetitive behavior and restricted interests were first described by Kanner (Autism, 1943) and Asperger (Asperger’s syndrome; 1944) in the mid-20th century. Between 1994 and 2013, autism and Asperger’s syndrome were distinguished mostly by early speech delay or major language alterations (Wing, 1981). Language level, however, is currently considered to be a continuous, rather than categorical variable (APA, 2013). The two conditions were merged into one disorder, the autism spectrum (AS), in DSM-5 for several reasons: disagreement among experts about the differences between Autism and Asperger (Lord et al., 2012); the inapplicability of DSM-IV Criteria because a diagnosis of autism was favored over Asperger’s syndrome in most cases (Mayes et al., 2001); similarities in adaptive outcome between the two conditions (Howlin, 2003); and the lack of reliable biomarkers (Macintosh and Dissanayake, 2004). Language level is now one of the four most heterogeneous components within the AS, together with associated medical conditions, intelligence, and adaptive level in DSM-5.

Studies that group individuals according to clinically-defined DSM-IV AS subgroups report no differences in cognition (Miller and Ozonoff, 2000; Wilson et al., 2014) or brain structure (McAlonan et al., 2008; Via et al., 2011) between Autism and Asperger syndrome. However, if individuals are divided according to clear categorical distinctions such as speech delay, then large differences can be observed between the two groups, for example, in processing speed (Barbeau et al., 2013) and in visual motion perception and performance in pursuit tasks (Takarae et al., 2008). Differences in perceptual processing are probably the most
replicated finding: AS groups with or without early speech delay perform differently in visual saccade and motion discrimination tasks (Takae et al., 2008; Takae et al., 2004) and only AS individuals with speech delay display auditory (Bonnel et al., 2010; Jones et al., 2009) or visual (Barbeau et al., 2013) abilities. Furthermore, differences in gray matter volume between AS individuals with or without speech delay have also been reported within regions associated with auditory and language processing, such as the middle temporal gyrus (Lai et al., 2014). The aim of this study was to search for group differences in brain activity during an auditory perception task and brain volume differences that may explain phenotypic heterogeneity in speech development among AS individuals.

2. Methods

2.1. Participants

Participants were recruited from the database of the specialized clinic for Pervasive Developmental Disorders at the Rivière-des-Prairies Hospital (Montréal, Canada). All individuals had been diagnosed with AS and satisfied autism DSM-IV criteria according to the Autism Diagnostic Observation Schedule (ADOS-C) (Lord et al., 1994), the Autistic Diagnostic Observation Schedule (ADOS-G module 3 or 4) (Lord et al., 1989) and multidisciplinary testing conducted by an experienced clinician (LM). Autistic participants differed only in terms of speech onset delay, to avoid the following confounding factors: 1) group differences in severity, which favor Type 1 between-group errors (Macintosh and Dissanayake, 2004); 2) uncertainty associated with the clinical assessment of Asperger syndrome; and 3) the treatment of differences between autism and Asperger syndrome as a continuous variable, which favors Type 2 errors (McAlonan et al., 2009). AS participants were divided into two groups based on the presence (AS-SOD) or absence (AS-NoSOD) of ADI-R criteria for Speech Onset Delay. Speech acquisition was considered typical if the first single words were reported by parents before 24 months of age and first two-word phrases before 33 months of age. Thirteen participants had speech onset delay and 14 did not. Exclusion criterion for the AS group included current use of psychoactive medication and neurological abnormalities. Thirteen typically developing individuals (TYP) were also included as controls in this study. The three groups were similar in terms of age, Full Scale, Verbal and Performance Wechsler IQ scored according to Canadian norms (Wechsler, 1991, 1997), sex ratio and terms of age, Full Scale, Verbal and Performance Wechsler IQ scored according to Canadian norms (Wechsler, 1991, 1997), sex ratio and handedness (Table 1). In addition, ADI-R scores were matched between AS-SOD and AS-NoSOD groups to ensure that the autistic phenotype was similar between the groups. All participants had normal hearing and no formal musical training. Informed written consent was obtained from all participants, or from the parents of participants under the age of 18, in accordance with the Regroupement Neuroimagierge Quebec ERB approved protocol #2006-0204. All participants were compensated for their participation.

2.2. Materials and procedure

Eight sound conditions were defined by crossing two carrier signals, pure tone (300 Hz), and harmonic tone (300 Hz, 600 Hz, 900 Hz, 1200 Hz), with four levels of frequency modulation, FM 0%, FM25% (±12.5 Hz), FM50% (±25 Hz), and FM100% (±50 Hz), at a modulation rate of 5 Hz. This modulation increment was selected because it results in a sustained auditory cortical response (Hall et al., 2003) and because low modulation rates are thought to be essential for speech recognition (Hall et al., 2002; Hougtast and Steeneken, 1985). These stimuli were also chosen for two reasons: first, because they highlight differences in patterns of brain activity associated with processing different levels of auditory complexity between autistic and non-autistic individuals, as reported previously by Samson et al. (2011); and second, to examine differences in the cortical auditory response between AS individuals with or without delayed speech onset (not dependent on auditory complexity), which was the objective of this study.

While lying in the scanner, the participants performed a controlled listening task in which they were required to detect the presence or absence of FM to ensure that they were actively listening to the stimuli, which generally results in greater and more reliable auditory cortical activity than that resulting from passive listening protocols (Hall et al., 2000). Stimuli were presented binaurally through MRI-compatible earphones at a mean sound pressure level (SPL) of 85–90 dB. A sparse sampling protocol with an effective TR of 9 s was used to present auditory stimuli in a silent background, thus minimizing perceptual interference from magnetic gradient noise and improving the detection of auditory cortex activity (Hall et al., 1999). Echoplanar images were acquired during three 10.8 min runs of 72 volumes each (TR = 2.76s, voxel size = 3.4 mm3). In each trial, a 6.24s auditory stimulus was presented before 2.76s of silence, during which image acquisition occurred. An anatomical T1-weighted high-resolution image was acquired with an MPRAGE sequence. Participants remained in the scanner for 50 min. Further details regarding the stimuli and task as well as the complete details of the imaging sequences used are provided in supplementary material.

2.3. Data analysis

Behavioral reaction time and accuracy data for the detection task were analyzed by two repeated-measures ANOVAs with Group (three levels) as a between-subject factor and Conditions (eight levels) as a within-subject factor. SPM8 was used for image preprocessing and statistical modeling. Images from the individual runs were realigned, unwarped, spatially normalized to the ICBM152 MNI space (Collins

| Table 1 | Socio-demographic characteristics of participants. TYP: Typically developing controls. SOD: Autistic individuals with speech onset delay. AS-NoSOD: Autistic individuals with no speech onset ADI-R: Autism Diagnostic Interview – Revised. |
|---------|---------------------------------|-----------------|------------------|------------------|-----------------|-----------------|-----------------|-----------------|
|         | TYP                             | SOD             | NoSOD            | p                |
| Sample size (sex) | 13 (2 F, 11 M) | 13 (2 F, 11 M) | 14 (1 F, 13 M) | 0.897            |
| Age (y/m)         | Mean (SD) | 23.6 (7.5) | 22.3 (6.8) | 22.11 (6.7) | 0.975            |
| Range            | 16–39               | 14–35            | 14–32            | 0.353            |
| Full-scale IQ    | Mean (SD) | 109.6 (10.3) | 101.4 (15.2) | 106.8 (16.5) | 0.353            |
| Range            | 92–131             | 78–130            | 82–129            | 0.422            |
| Mean (SD) | 106.3 (12.5) | 105.8 (12.4) | 100.8 (14.2) | 0.422            |
| Range            | 87–133             | 91–131            | 77–126            | 0.052            |
| Mean (SD) | 111.1 (10.2) | 97.5 (16.7) | 111.1 (16.4) | 0.052            |
| Range            | 93–127             | 72–124            | 81–132            | 0.975            |
| Handedness       | Mean (SD) | +61.2 (39.3) | +65 (53.1) | +62 (64.0) | 0.975            |
| Range            | -45 to 100       | -100 to 100       | -80 to 100        | 0.921            |
| ADI-R Score Mean (cut-off) | 23.9 (10) | 22.2 (10) | 0.186            |
| Social Communication | 18.2 (8) | 16.1 (8) | 0.921            |
| Behavior         | 6.9 (3)           | 6.7 (3)           | 0.261            |
et al., 1994), and spatially smoothed with a 3D Gaussian filtering kernel of 9 mm FWHM. First level analyses were conducted for each participant with a design matrix containing the eight stimulus conditions, along with six head motion estimates that were included as covariates of no interest. Each stimulus condition was compared with the silence baseline condition to generate first-level contrast images (eight per participant). These first-level contrasts were then included in a mixed effect model with three factors: Participant (40 levels), Group (three levels; assumed to have unequal variance) and Task (eight levels).

First, for each group, weighted contrasts combining the contrasts of each sound condition minus the silence baseline were computed. Second, between-group contrasts were defined to investigate the differential effects of combining the contrasts of each sound condition minus silence. T-contrasts were defined to compare group effects between (1) TYP and AS-SOD, (2) TYP and AS-NoSOD and (3) AS-SOD and AS-NoSOD groups within the regions showing task-related activity. A corrected Family Wise Error critical threshold ($p_{FWE} < 0.05$) with 50 contiguous voxels (170 mm$^3$) was used.

A voxel-based morphometry (VBM) analysis (SPM8 VBM-DARTEL; Ashburner, 2010) was also performed to confirm that regional group differences observed in the patterns of functional activity were not related to gray matter volume. A one-way ANOVA was performed to examine group differences in gray matter volume for the whole-brain and in regions where differences in activity between groups were observed ($p_{FWE} < 0.05$). Further details regarding data analysis are given in supplementary material.

3. Results

3.1. Behavior

As expected, Group had no effect on accuracy ($p = 0.932$) or response times ($p = 0.165$), and there was no interaction between Group and Task for accuracy ($p = 0.882$) or response time ($p = 0.621$). Accuracy was high (mean of 87%, 88% and 89% accurate responses for the TYP, AS-SOD and AS-NoSOD groups, respectively) indicating that all participants listened carefully to the presented stimuli and could detect the frequency modulation.

3.2. Imaging — fMRI results

3.2.1. Main effect analysis

Task and Group showed significant main effects in fMRI, but no Task-by-Group interaction was observed. Brain activity in the bilateral auditory cortex during the task was measured with 1581 voxels on the right and 1288 voxels on the left centered on primary auditory cortex (BA 41) and extending to the non-primary superior temporal auditory fields (BA 22).

The three groups showed similar strong task-related activity for all auditory stimuli and there was no significant interaction between task and group. Large portions of the cortical surface showed activity in fMRI, including the auditory cortex, (transverse temporal (BA 41, 42) and superior temporal (BA 22) gyri), peri-auditory regions (middle temporal (BA 21) and posterior superior temporal (BA 22) gyri), as well as regions associated with language processing like the inferior frontal (BA 44, 45) and supramarginal (BA 40) gyri. For the detection task, activity was also observed in cortical regions associated with the motor response, including the somatosensory cortex (postcentral gyrus; BA 2, 3), premotor region (superior and medial frontal gyri; BA 6) and the primary motor cortex (precentral gyrus; BA 4). All three groups also showed task-related activity in the prefrontal cortex (BA 46), the superior parietal lobule (BA 7) and the cerebellum (Fig. 1, Supplementary Table 1).

3.3. Between-group differences

3.3.1. TYP vs. AS-SOD

Cortical regions associated with the motor response were more active in the TYP group than in the AS-SOD group. These regions included the primary somatosensory region (postcentral; BA 2, 3), the primary motor cortex (precentral gyri; BA 4, more active on the left than on the right) and the bilateral premotor and supplementary motor area (superior frontal gyrus, BA 6). Activity was also higher in the TYP group than in the AS-SOD group in several other regions: the prefrontal cortex (bilateral middle frontal gyrus; BA 9,
10, 46), the left cingulate gyrus (BA 31, 32), both of which are involved in language processing, as well as the right inferior frontal gyrus (BA 44) and bilateral supramarginal gyrus (BA 40), and subcortical structures, namely the thalamus and the cerebellum. Conversely, the AS-SOD group displayed stronger activity than the TYP group in auditory regions. In particular, AS-SOD individuals showed peaks of activity in the right superior temporal gyrus (BA 22) which extended into the left insular cortex (BA 13) and the transverse temporal gyrus (a significant peak of activity [52, –26, 6; t = 4.45] was observed when using a small volume correction analysis (BA 41)). These differences in activity are shown in \( \text{Fig. 2A} \) (Supplementary Table 2).

### 3.3.2. TYP vs. AS-NoSOD

Task-related activity was higher in the TYP group than in the AS-NoSOD group in the left auditory cortex (transverse temporal gyrus; BA 41) and in bilateral motor regions, specifically in the primary motor cortex (BA 4) and the supplementary motor area (superior frontal gyrus; BA 6). In addition, the TYP group showed more activity than the AS-NoSOD group in the somatosensory cortex (postcentral gyrus; BA 2), the right prefrontal cortex (middle frontal gyrus; BA 46), the right inferior parietal lobule (BA 40), left insula (BA 13), the left transverse temporal gyrus (BA 41) and both hemispheres of the cerebellum. By contrast, the AS-NoSOD group showed greater activity than the TYP group in language-related regions, including bilateral Broca’s area (inferior frontal gyrus; BA 44) and the bilateral supramarginal gyrus (BA 40), and in peri-auditory regions, including the middle temporal (BA 21) and superior temporal (BA 22) gyri. The AS-NoSOD group also showed more activity in the premotor (BA 6) and somatosensory cortex (BA2), which are located in front of the regions showing more activity in the TYP group. The AS-NoSOD group also displayed greater activity in the superior parietal lobule (BA 7), the left prefrontal cortex (middle frontal gyrus; BA 46), the right superior cerebellum and bilateral putamen. Differences in activity between the TYP and the AS-NoSOD groups are presented in \( \text{Fig. 2B} \) (Supplementary Table 2).

### 3.3.3. AS-SOD vs. AS-NoSOD

The AS-SOD group showed greater activity than the AS-NoSOD group only in one cluster encompassing the right auditory cortex, specifically in the transverse temporal gyrus (a significant peak of activity [58, –20, 6; t = 6.61] was observed when using a small volume correction analysis (BA 41)) and the superior temporal gyrus (BA 22). Conversely, the AS-NoSOD group displayed stronger task-related activity than the AS-SOD group in many brain regions. This included bilateral activity in regions associated with language processing, specifically Broca’s area (inferior frontal gyrus BA 44, 45) and the supramarginal gyrus (BA 40), as well as the peri-auditory cortex, mainly the middle temporal (BA 21) and the anterior portion of the superior temporal gyri (BA 22). The AS-NoSOD group also displayed greater activity in the primary somatosensory cortex (postcentral gyrus; BA 2, 3) and the premotor (medial frontal gyrus; BA 6) and primary motor cortex (precentral gyrus; BA 4), all of which are involved in the motor response. Finally, the AS-NoSOD group had greater task-related activity than the AS-SOD group in the prefrontal cortex (middle frontal gyrus; BA 46), the bilateral superior parietal cortex (BA 7), the left cingulate gyrus (BA 31), the right cuneus (BA 17) as well as the hippocampus, putamen, and cerebellum. The regions showing differential task-related activity in the AS-SOD and the AS-NoSOD groups are shown in \( \text{Fig. 2C} \) (Supplementary Table 2).

### 3.4. Imaging — VBM results

Whole-brain and regional gray matter volume were similar between groups. Thus, either the power of the analysis was too limited to observe differences or gray matter volume does not explain group differences in the patterns of functional activity.

### 4. Discussion

#### 4.1. Typical function of the regions showing between-group differences

Brain regions that showed higher activity in the AS-SOD than in the AS-NoSOD group are related to low-level auditory cortical processing, as shown by the overlap between these regions and the areas that are consistently reported in fMRI studies examining responses to auditory stimuli (Fig. 3, Automated meta-analysis of 84 studies, Neurosynth.org). These regions (Heschl’s gyrus, the lateral superior temporal gyrus) are involved in the extraction of basic acoustic features such as frequency and changes to temporal or amplitude modulation (Hart et al., 2003; Samson et al., 2010; Wessinger et al., 2001), and are also thought to be important for...
the first stages of speech processing (Hall et al., 2003; Scott and Johnsrude, 2003).

By contrast, regions that showed higher activity in the AS-NoSOD than in the AS-SOD group were related to higher-level processes. Most of these regions are associated with language and voice processing, as shown by the overlap between these regions and those identified by the meta-analysis shown in Fig. 3 (Automated meta-analysis of 725 studies for 'language' and 81 studies for 'voice', Neurosynth.org). The AS-NoSOD group showed greater activity in regions further down the hierarchical auditory and language cortical path, mainly the inferior frontal gyrus (Broca’s area), which processes intelligible and complex speech (Davis and Johnsrude, 2003; Peelle et al., 2010; Samson et al., 2010), and the middle temporal gyrus, which is involved in phonemic and lexical processing, notably the processing of isolated syllables (Liebenthal et al., 2005) and words (Binder et al., 2000; Price et al., 1992). This region specifically responds to vocal (speech or non-speech) sounds (Belin et al., 2000; Samson et al., 2010).

Interestingly, VBM analysis revealed no differences in cortical volume between groups, despite differences in activity. Previous studies have reported significant anatomical differences between AS individuals with or without speech delay within some of the regions showing differences in activity in our study (i.e. the middle temporal gyrus); however, these findings are only relevant for groups with significantly different social abilities, which was not the case in our study (Lai et al., 2014). Therefore, we argue that neural networks are functionally reorganized in AS to favor sensory or perceptual processing in individuals with AS-SOD and language processing in those with AS-NoSOD.

In addition, AS-NoSOD individuals showed greater activity than TYP individuals in regions associated with motor functions, as shown by the overlap between these regions and those identified in an automated meta-analysis of 303 fMRI studies examining activity in the motor cortex (Fig. 4). Thus, in AS-NoSOD individuals, motor areas may be ‘recycled’ and used for auditory cognition (i.e. evolutionarily old brain circuits are allocated another function (Dehaene and Cohen, 2007)), which may explain why these individuals show clumsiness (Mottron et al., 2014).

4.2. Interpretation of between-group differences in activity

In AS-SOD individuals, overall activity in language-related regions was low, whereas activity was high in perceptual auditory brain regions. Enhancement in perceptual auditory regions is consistent with the exceptional ability of AS-SOD individuals to discriminate pitch, which is one of the most replicated findings in research on autism (O’Connor, 2012). The data from our study do not show whether AS-SOD individuals have exceptional pitch processing; however, superior pitch is typically specific of this subgroup, as we reported previously (Bonnel et al., 2010) in a cohort containing 54–62% of the individuals included in the current study (seven out of 13 TYP, eight out of 13 SOD and eight out of 14 No-SOD participants in our study were also included in (17)). Similarly, AS-SOD individuals showed superior pitch processing in another cohort containing five out of the 13 AS-SOD individuals from the current study (Meilleur et al., 2014). Conversely, regions associated with language processing were less active in AS-SOD than in TYP individuals. Perceptual strengths in the AS, either visual (block design peak score, superior visual inspection time, visually presented non-verbal reasoning) or auditory (pitch discrimination) are frequently associated with a delay, deficits or
abnormalities in speech (Caron et al., 2006; Heaton et al., 2008; Jarvinen-Pasley and Heaton, 2007). In addition, visual perceptual areas also play an important role in AS-SOD individuals. Indeed, AS-SOD individuals showed higher activity than controls in the extrastriate cortex (BA 18) during a visual reasoning task (Raven's Standard Progressive Matrices; Soulieres et al., 2009). Furthermore, performance in various perceptual tasks co-varies between autistic individuals, indicating that it depends on a single domain-general factor (Meulier et al., 2014). Language capacities that are preserved in AS-SOD individuals, as well as special language abilities, mostly involve the perceptual processing of language: for example, reading or reproducing a phonological sequence (Grigorenko et al., 2003) or the use of language labels to map the environment (Walesinski et al., 2008).

By contrast, cortical areas associated with language processing are highly active in AS-NoSOD individuals during both the perception of non-social auditory material and frequency-modulated sounds (non-modulated conditions were not included in the analysis), which possess speech-like, acoustic properties (Hall et al., 2002; Houtgast and Steeneken, 1985). Thus, AS-NoSOD individuals process the acoustic components relevant to speech recognition better than non-autistic individuals. These findings are consistent with the IQ profile of AS-NoSOD individuals. Indeed, a meta-analysis of differences in IQ profiles between AS-SOD and AS-NoSOD individuals revealed that VIQ is generally higher than PIQ in AS-NoSOD (Chiang et al., 2014). Similarly, the average VIQ of our AS-NoSOD individuals was 111 and their average PIQ was 101. The AS-NoSOD group also performed, on average, two scaled score points above average on the vocabulary and similitude subtests of the WAIS, consistent with other reports (Nader et al., in press). They developed language skills quickly, and spoke their first word at an average of 14 months of age. However, AS-NoSOD individuals do not display the visuospatial strengths characteristics of AS-SOD (Nader et al., in press). They also favor the use of language strategies when solving problems (Sahyoun et al., 2009). Clinically, the overuse of language by AS-NoSOD individuals sometimes manifests as extreme verbosity (Adams et al., 2002), and their “categorical”, verbally-defined restricted interests (Mottron et al., 2013).

In summary, the differences between AS-SOD, AS-NoSOD and TYP individuals arise from the use of a perceptual or language approach to processing auditory information. According to the enhanced perceptual functioning model (Mottron et al., 2006), loci of atypical activity can classify autistic individuals into subgroups. The division of language into perceptual and linguistic components explains why some language components in the AS-SOD group are defective whereas others are over-functioning. The perceptual processing of speech in AS-SOD individuals may account for echolalia, their outstanding ability to discriminate pitch in speech, early decoding strengths, and the occurrence of speech delay with perceptual strengths. By contrast, in AS-NoSOD individuals, a more recent model (Mottron et al., 2014) suggests that incoming information is primarily processed by the over-functioning of typical language-related processes, resulting in language strengths, but not perceptual ones. Thus, AS-NoSOD involves the overdevelopment of language functions, both in terms of performance and brain activity.

4.3. Reinterpreting the DSM-IV and the distinction between Autism and Asperger syndrome

Our findings suggest that AS-NoSOD cannot simply be considered to be "AS with language preserved", and/or a milder phenotype somewhere between autism and normal development. Instead, AS-NoSOD, which is the best description of what was identified as Asperger syndrome in the DSM-IV, is characterized by enhanced language development, processing and production, as shown by the early achievement of speech milestones, and strong performance in verbal subtests (Nader et al., in press). By contrast, auditory perception in AS-SOD is not only preserved, it is enhanced (O'Connor, 2012), and is associated with major speech alterations, as reported in a study on pitch discrimination (Bonnel et al., 2010) including more than half the participants from the current study. Although we did not investigate pitch processing performance here, previous studies show that auditory perceptual processing is stronger in AS-SOD than in TYP individuals and may be associated with high levels of activity in auditory cortical regions in AS-SOD individuals. Delayed speech onset appears to be associated with the “perceptual learning” of language in AS-SOD individuals, because they favor written over oral material and may develop echolalia (Mottron et al., 2013 for a review). Thus, our findings show that major differences in neurocognitive organization can be identified when individuals are distinguished according to speech onset rather than their current language level.

The location of activity in regions that are typically more plastic in non-autistic individuals is highly variable in autistic individuals, which is called “ectopic brain activity” in autism (Poulin-Lord et al., 2014). Our results extend this finding, which has been convincingly demonstrated in the visual domain, to the auditory and language domain. Ectopic brain activity has also been reported during a visuomotor sequence learning task (Muller et al., 2004, 2003) and in the fusiform gyrus during facial processing (Pierce et al., 2001; Scherf et al., 2010). Our findings also suggest that fMRI differences between autistic groups may result from the alternative use of distinct brain regions during tasks.

According to the ‘Target’ component of the ‘Trigger-Threshold-Target’ model (Mottron et al., 2014), autism develops as a result of a plastic reaction targeting the most variable cortical regions. This reaction may target either one of the two domain-general regions because they are evolutionarily and developmentally similar. In AS-SOD, the associative perceptual cortex is affected, whereas in AS-NoSOD, language regions are affected. The DSM-IV subgroups “Autism” and “Asperger syndrome” were recently merged into the same DSM-5 category, the “AS”. Our results show that this new classification system is consistent with the presence of cortical plasticity in both cases, which is related to superior domain-specific activity and performance. However, our findings suggest that particular DSM-V clinical specifiers of the AS, such as ‘language level’, may classify individuals with substantially different neurocognitive organization.

4.4. Perspectives

The differences that we report in patterns of brain activity between AS—SOD and AS-NoSOD may limit the interpretation of differences between autistic and non-autistic individuals in studies in which autistic individuals are included in a single group. The average direction of group differences in activity during auditory tasks involving autistic individuals may accordingly depend on the ratio of individuals with or without SOD in the group under study. Our inclusion criteria for autistic participants were designed to make a clear-cut distinction between AS-SOD and AS-NoSOD. Therefore, our findings may not be relevant for autistic individuals who have not been distinguished according to this subgrouping, such as those presenting with comorbid dysphasia, subthreshold individuals, and clinically-defined Asperger syndrome.

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Contributors
All the coauthors have contributed significantly to this study. F.S., L.M. and T.A.Z. conceived and designed the study. F.S. acquired the data, F.S., H.B., J.D. and T.A.Z. contributed to data analysis and L.M. and F.S. interpreted the data. All authors made substantial contribution to drafting the article or reviewing it critically. All authors gave final approval of the version of the article to be published and can certify that no other individuals not listed in the authors have made substantial contributions to the paper.

Conflict of interest
We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work.

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Appendix A Supplementary data
Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jspysci.2015.05.011.

References
Ashburner J. VBM Tutorial. 2010.
Ashburner J, Friston KJ. Modulation and task effects in auditory processing measured using fMRI. Hum Brain Mapp 1999;7:213–23.


