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Abnormal processing of emotional prosody in Williams syndrome: An event-related potentials study

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A R T I C L E   I N F O

A B S T R A C T

Williams syndrome (WS), a neurodevelopmental genetic disorder due to a microdeletion in chromosome 7, is described as displaying an intriguing socio-cognitive phenotype. Deficits in prosody production and comprehension have been consistently reported in behavioral studies. It remains, however, to be clarified the neurobiological processes underlying prosody processing in WS.

This study aimed at characterizing the electrophysiological response to neutral, happy, and angry prosody in WS, and examining if this response was dependent on the semantic content of the utterance. A group of 12 participants (5 female and 7 male), diagnosed with WS, with age range between 9 and 31 years, was compared with a group of typically developing participants, individually matched for chronological age, gender and laterality. After inspection of EEG artifacts, data from 9 participants with WS and 10 controls were included in ERP analyses.

Participants were presented with neutral, positive and negative sentences, in two conditions: (1) with intelligible semantic and syntactic information; (2) with unintelligible semantic and syntactic information ('pure prosody' condition). They were asked to decide which emotion was underlying the auditory sentence.

Atypical event-related potentials (ERP) components were related with prosodic processing (N100, P200, N300) in WS. In particular, reduced N100 was observed for prosody sentences with semantic content; more positive P200 for sentences with semantic content, in particular for happy and angry intonations; and reduced N300 for both types of sentence conditions.

These findings suggest abnormalities in early auditory processing, indicating a bottom-up contribution to the impairment in emotional prosody processing and comprehension. Also, at least for N100 and P200, they suggest the top-down contributions of semantic processes in the sensory processing of speech. This study showed, for the first time, that abnormalities in ERP measures of early auditory processing in WS are also present during the processing of emotional vocal information. This may represent a physiological signature of underlying impaired on-line language and socio-emotional processing.

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1. Introduction

Williams syndrome (WS), a genetic neurodevelopmental disorder due to microdeletion in chromosome 7, has been described a syndrome with an intriguing socio-cognitive phenotype (Bellugi, Bihrle, Neville, Jernigan, & Doherty, 1992; Bellugi, Lichtenberger, Mills, Galaburda, & Korenberg, 1999; Bellugi, Marks, Bihrle, & Sabo, 1988; see Martens, Wilson, & Reutens, 2008 for a review).

The initial descriptions of individuals with WS made reference to their apparently preserved abilities of linguistic expression, as exemplified by complex and elaborated narratives along with an intense interest in being engaged in social communication (e.g., von Arnim & Engel, 1964). However, this keen interest in engaging in social interactions (coupled with an overfriendly personality and empathic behavior) tends to coexist with severe pragmatic impairments (Laws & Bishop, 2004), such as the difficulty to adjust the amount of speech production to the listener's interests and attitudes. For example, some narrative studies suggest that participants with WS use significantly more affective expressive prosody than individuals with Down syndrome and typically developing children (Gonçalves et al., 2004, 2010; Jones et al., 2000; Reilly, Klima, & Bellugi, 1991; Reilly, Losh, Bellugi, & Wulfeck, 2004), and that this pattern seems to be independent of the audience and on how many times they tell the story. In other words, the frequent use of dramatic devices and social hookers, used to capture the attention of the audience, may have been masking WS individuals' deficits in understanding social cues (Skwerer, Schofield, Verbalis, Faja, & Tager-Flusberg, 2007). This is corroborated by studies showing difficulties in effective deployment and interpretation of paralinguistic devices as illustrated by difficulties in theory-of-mind tasks (e.g., Sullivan & Tager-Flusberg, 1999; Tager-Flusberg & Sullivan, 2000), and deficits in the identification and discrimination of emotions (e.g., Catterall, Howard, Stojanovik, Szczerbinski, & Wells, 2006; Plesa-Skwerer, Faja, Schofield, Verbalis, & Tager-Flusberg, 2006; Tager-Flusberg & Sullivan, 2000), particularly negative emotions (Plesa-Skwerer et al., 2006).

One of the powerful paralinguistic cues routinely employed in verbal communication is prosody. Emotional prosody represents a paralinguistic device that allows human beings to represent and convey affect (Scherer, 1986). It relies on language suprasegmental features such as fundamental frequency (F0), sound intensity and duration (Hesling, Clément, Bordessoules, & Allard, 2005; Kotz & Paulmann, 2007; Wildgruber, Ackermann, Kreifelts, & Ethofer, 2006). The perception of emotional prosody is a multi-stage process that consists of (1) the analysis of acoustic features of spoken words, (2) deriving emotional significance from acoustic cues, (3) applying it in higher cognition operations, and (4) integrating emotional prosody in language processing (Hoekert, Bais, Kahn, & Aleman, 2008; Schirmer & Kotz, 2006; Wildgruber et al., 2006). Thus, the study of prosody processing may provide us with information on how individuals recognize and interpret sensory input (e.g., voice inflection), an ability that is crucial to social interactions and, in particular, to social reciprocity.

Behavioral studies on prosody processing in WS have found deficits in prosody comprehension (Catterall et al., 2006; Plesa-Skwerer et al., 2006; Skwerer et al., 2007), suggesting that, in spite of an easy sociability, these individuals may be impaired in their ability to use vocal cues to interpret emotional states particularly in the presence of a semantic conflict such as sarcasm or irony (Skwerer et al., 2007; Sullivan, Winner, & Tager-Flusberg, 2003). However, in spite of their difficulties in using prosody for semantic processing, individuals with WS still seem to perform better than participants with learning or intellectual disabilities on the recognition of emotional tone of voice in filtered speech (Plesa-Skwerer et al., 2006), suggesting that sensitivity for non-linguistic affective information may be relatively spared in WS. This seems to be consistent with the unusual profile of auditory processing that characterizes WS, which includes a keen interest in music and musical activities (Hopyan, Dennis, Weksberg, & Cytrynbaum, 2001; Levitin & Bellugi, 1998; Udwin, Yule, & Martin, 1987).

In spite of the few studies devoted to prosody processing in WS reviewed above, there is a dearth of data on this issue, in contrast to the number of studies focusing on the morphosyntactic and semantic aspects of language processing in WS individuals.

Importantly, electrophysiological studies of prosody processing in WS are, to the best of our knowledge, nonexistent. Due to their temporal resolution, Event Related Potentials (ERPs) (Coles & Rugg, 1995; Münte, Urbach, Düzel, & Kutas, 2000) provide valuable information on the order of msec about cognitive processes under consideration. As such, they afford a window of enquiry into the neural underpinnings of sensory and cognitive processes associated with prosody processing in WS.

ERP studies in normal individuals show that prosody comprehension has distinct electrophysiological signatures (e.g., Kotz & Paulmann, 2007; Paulmann & Kotz, 2008a; Paulmann & Kotz, 2008b; Paulmann, Seifert, & Kotz, 2010). Most studies examined interactions between semantics and prosody and these studies often used a 'prosody violation' approach where juxtapositions between two intonational patterns, or between semantics and prosody, were investigated. These studies reported late occurring negativities and positivities that indexed processing incongruities between the prosody in the initial and the final part of the sentence (e.g., initial happy prosody ending with sad prosody) or between semantics and prosody. For example, expectancy violations of integrative emotional prosodic and semantic information elicited a more negative-going component in the time window between 450 and 650 ms, while expectancy violations of emotional prosodic information were linked to a more positive-going component in the time window between 700 and 1000 ms, in a task using a cross splicing technique (Paulmann & Kotz, 2008a).

However, studies using naturalistic designs (i.e., in sentences delivered with either neutral or emotional intonation without artificially introducing discrepancy between sentence fragments, or between message and the tone with which it was delivered) are few. The existing ones (Paulmann & Kotz, 2008b; Paulmann et al., 2010) suggest that the differentiation of basic vocal emotional expressions from prosodically neutral sentences occurs around 200 ms, with emotional sentences eliciting less positive P200 amplitudes, irrespective of valence (positive vs. negative) (Paulmann & Kotz, 2008b). According to

these authors, P200 reflects an automatic and early detection of emotional salience in the acoustic signal, which is followed by the integration of its features with verbal (e.g., semantic) information and by the cognitive evaluation of its emotional significance (see Schirmer & Kotz, 2006).

It is worth noting that P200 and N100 are two relevant components elicited by auditory stimuli, although in these previous studies on prosody processing (Paulmann & Kotz, 2008b; Paulmann et al., 2010) N100 has not been analyzed. The auditory N100 component is believed to reflect sensory and perceptual processing and to be modulated by attention (Hillyard, Hink, Schwent, & Picton, 1978; Näätänen, Gaillard, & Mäntysalo, 1978; see Rosburg, Boutros, & Ford, 2008 for a review). P200 is related to early stimulus encoding, reflecting attentional mechanisms and stimulus detection or classification (Picton & Hillyard, 1974). It has been argued that P200 is a separate component, sensitive to overlapping but not identical parameters with N100 (Crowley & Colrain, 2004). More recently, P200 has been associated with encoding emotional significance of speech (Paulmann & Kotz, 2008b; Paulmann et al., 2010).

The aim of the current study was to provide initial evidence regarding the electrophysiological correlates of prosody processing in a group of individuals with WS, taking advantage of the ERP methodology, and especially of its temporal resolution. More specifically, we aimed at: (1) characterizing the electrophysiological responses (ERP) elicited by three emotional intonation patterns; and (2) examining whether the ERP response was modulated by the semantic content of the utterance. Given the relative paucity of ERP studies on prosody processing, the research questions fell into two categories: those related to ERP correlates of prosody processing irrespective of group membership and those focused on electrophysiological differences in prosody processing between the two groups (WS and normal individuals). The specific *a priori* hypotheses were:

(1) Our central hypothesis concerned group differences between WS and typically developing (TD) individuals.
(2) Based on previously published studies Paulmann and Kotz (2008b), we predicted that neutral and emotional prosodic sentences would be differentiated in the early (N100 and P200) components. Given the reported heightened sensitivity to positive social cues in WS (e.g., Haas et al., 2009) and the reduced reactivity to negative social signs (Haas et al., 2009; Meyer-Lindenberg et al., 2005), we expected increased P200 amplitude to happy prosody and reduced P200 to angry intonations in WS relative to a typically developing control group.
(3) Based on previously published studies (Kotz et al., 2003; Kotz & Paulmann, 2007; Paulmann & Kotz, 2008b), we predicted that there would be differences in processing sentences as a function of their semantic content. That is, we predicted that comparable emotional prosody sentences would be processed in different ways depending on whether they carry both semantic and prosodic information or prosodic information only.

Previous studies (Mills et al., 2003; Neville, Mills, & Bellugi, 1994) found sensory abnormalities in WS. However, it is also possible that these abnormalities are further exacerbated by abnormalities in higher order cognitive functions, such as semantic processing. If N1-P2 abnormalities are limited to sentences with semantic content, this would suggest that the modulation of sensory processes by higher order operations is necessary for observing abnormalities at initial stages of prosody processing in WS. Adopting the hypothesis of preserved sensitivity to "pure" affective prosody (Plesa-Skwerer et al., 2006), we predicted that group differences would be found for sentences with semantic content but not for sentences without it ('pure prosody' sentences).

In order to address these hypotheses, 12 participants with WS and 12 typically developing individuals were presented with three types of sentences (neutral, positive and negative prosody), in two conditions: (1) with intelligible semantic and syntactic information; (2) with unintelligible semantic and syntactic information.

2. Methods

2.1. Participants

A group of 12 participants (5 female and 7 male), diagnosed with Williams Syndrome, with age range between 9 and 34 years ($M = 17.3$, $SD = 6.50$), was compared with a typically developing group (12 participants), individually matched for chronological age ($M = 17.3$, $SD = 6.50$), gender, and handedness (see Table 1).

Participants with WS were recruited at a large Genetic Medical Institute in Oporto, Portugal, and also in collaboration with the Portuguese Williams Syndrome Association. WS diagnoses were made by fluorescent in situ hybridization (FISH) confirmation of elastin gene deletion (Korenberg et al., 2000). Exclusion criteria included: (a) the presence of severe sensory (e.g., hearing problems) or speech disorder; (b) comorbidity with severe psychopathology not associated with the syndrome;

Table 1
Demographic characteristics of the participants – mean (*SD*).

	Mean (*SD*)	
	WS Group (*N* = 12)	TD Group (*N* = 12)
Age (years)	17.30 (6.49)	17.30 (6.49)
Parental SES	3.00 (1.28)	2.92 (1.44)
Years of education	7.58 (1.78)	10.83 (3.66)

Table 2
Results of the neurocognitive assessment of Williams Syndrome (WS) and Typically Developing (TD) groups.

	Mean (SD)		Significance test
	WS Group (N = 12)	TD Group (N = 12)	F (p)
1. Global intellectual functioning			
Verbal IQ	58.55 (9.18)	116.45 (14.75)	122.17 (.000**)
Performance IQ	52.18 (5.96)	111.73 (16.32)	129.15 (.000**)
Full Scale IQ	51.55 (7.10)	114.00 (13.71)	182.87 (.000**)
2. Language (Phonological processing)			
(a) Discrimination of Minimal Pairs in Pseudowords			
Similar pairs	31.44 (0.73)	31.92 (0.29)	4.24 (.053)
Different pairs	29.44 (3.71)	31.67 (0.49)	4.27 (.053)
(b) Auditory Lexical Decision and Morphology			
Regular words	12.38 (2.45)	14.67 (0.89)	8.98 (.008*)
Derived words	12.25 (3.24)	13.92 (1.31)	2.60 (.124)
Pseudowords	21.63 (7.98)	28.00 (4.20)	5.49 (.031*)
(c) Repetition of Pseudowords			
1 syllable	8.88 (1.13)	9.75 (0.45)	5.95 (.025*)
2 syllables	8.63 (2.07)	10.00 (0.00)	5.47 (.031*)
3 syllables	8.38 (0.92)	10.00 (0.00)	38.83 (.000**)

* $p < .05$.
** $p < .005$.

(c) use of any medication that might affect cognitive function or electroencephalogram (EEG) recordings, such as steroids and barbiturates; (d) and use of any psychoactive medication. Controls were typically developing individuals without evidence of psychiatric, neurological disorder or cognitive impairment. All participants were right-handed, according to the Edinburgh handedness inventory (Oldfield, 1971), and spoke European Portuguese as their first language. Each participant and their guardians (in the case of minor participants) gave written informed consent for their participation in the study, after a detailed description of the study. The Ethics Committee of the University of Minho approved this study.

The mean socioeconomic status, as measured by an adapted version of Graffar Scale (Graffar, 1956), with 5 being the highest and 1 being the lowest score, was 3.00 (SD = 1.28) for the WS group and 2.92 (SD = 1.44) for the typically developing control group (TD). Groups did not differ in socioeconomic status ($t(22) = -0.15$, $p > .05$), but did differ in years of education ($t(22) = 2.76$, $p = .011$).

To assess general cognitive functioning (Full Scale IQ), participants with chronological age between 9 and 16 years were administered the Portuguese version of the Wechsler Intelligence Scale for Children – Third Edition (WISC-III) (Wechsler, 1991), while participants over 16 years old were administered the Portuguese version of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) (Wechsler, 1997). Since the experimental task in this study was auditory, the following measures of auditory (phonological) processing were used, from the Portuguese version of Psycholinguistic Assessment of Language Processing in Aphasia – PALPA (Castro et al., 2007): Discrimination of Minimal Pairs in Pseudowords; Auditory Lexical Decision and Morphology, Repetition of Pseudowords. Neurocognitive tests were in the native language of the participants and were administered and scored accordingly. Results of general cognitive assessment are presented in Table 2.

Mean distribution of Full Scale Intelligence Quotient (FSIQ) in WS was found to be within the moderate mental retardation interval, with verbal intelligence quotient (IQ) slightly higher than performance IQ.

2.2. Stimuli

A set of 216 semantically neutral sentences, presented binaurally with angry, happy or neutral intonation, was used as stimuli in this experiment.

The sentences were developed using a validation study where a set of 157 actions (e.g., "to read a magazine", "to hurt the eye", "to hug a child") were presented to a sample of children and adolescents (N = 190) from different age groups (from 2nd grade to high school). Participants were asked to judge if these sentences were associated with an unpleasant, pleasant or neutral feeling. From this set, 60 actions rated by at least 95% of the subjects as "neutral" in semantic content were selected and 48 sentences were developed. Following the procedure used by Kotz et al. (2003), all sentences had the same syntactic structure (noun + verb + direct object) and length (4 words) and began with a personal pronoun (e.g., "She stirred the soup", "She fried an egg", "He opened the closet", "He peeled the banana"). Subsequently, they were recorded by a female native speaker of Portuguese with training in theatre techniques, each with a positive (happy), negative (angry and sad), or neutral intonation. The recordings were made in a sound proof room with an Edirol R-09 recorder and a CS-15 cardioid-type stereo microphone, using a sampling rate of 22 kHz and 16-bit quantization. Sentences were then digitized, downsampled at a 16 bit/16 kHz sampling rate and normalized in amplitude.

Sentences with sad intonation were included as fillers, in order to provide a broader range of options for the participants rating the sentences. The raters were children and adolescents (N = 125), from 4th to 9th grades, who judged the emotional intonation of the sentences. Thirty-six sentences of neutral, happy, and angry prosody with inter-rater agreement of at least 90% were then selected (31 for the experimental session and 5 for the training session). Sentences were pseudo randomly

Table 3
Acoustical analyses of the sentences presented in the experiment.

	Neutral	Happy	Angry
Mean duration	1.88 (0.18)	2.00 (0.16)	1.79 (0.13)
Fundamental Frequency (F0)	203.97 (5.11)	448.01 (33.16)	293.44 (32.51)
Intensity	80.00 (2.32)	77.00 (1.67)	77.00 (1.83)

Notes: F0 is measured in Hz; duration is measured in seconds. Numbers in parentheses show standard deviations.

distributed into three experimental lists to be presented as stimuli in the first part of the experiment (see Table 3). These sentences were intelligible, so that the participants could understand their semantic and syntactic content (Fig. 1).

The same stimuli were delexicalized and served as stimuli in the second part of the experiment. All the phonological and lexical information was suppressed but the prosodic modulations were kept (see Figs. 2 and 3). We hypothesised that stimuli with no lexical content should, as in previous studies, elicit prosodic effects that are not dependent of semantic information (Paulmann & Kotz, 2008a). The phonemes of each sentence were manually segmented in Praat (Boersma & Weenink, 1992–2008). The fundamental frequency (F0) was automatically extracted in Praat at four points of each segment (20%, 40%, 60% and 80%). Occasional F0 error measurements were manually corrected. Based on the procedures of Ramus and Mehler (1999), duration and F0 values were then transferred to MBROLA (Dutoit et al., 1996) for concatenative synthesis by using the European Portuguese (female) diphone database. In order to omit linguistic information and test the perception of different emotions by means of prosodic information, all fricatives were replaced with the phoneme /s/, all stop consonants with /t/, all glides with /j/, all stressed vowels with /æ/ and all unstressed vowels with /ə/. Thus, as in Ramus and Mehler (1999), the synthesis of the new sentences preserved "global intonation, syllabic rhythm, and broad phonotactics" (p. 514).
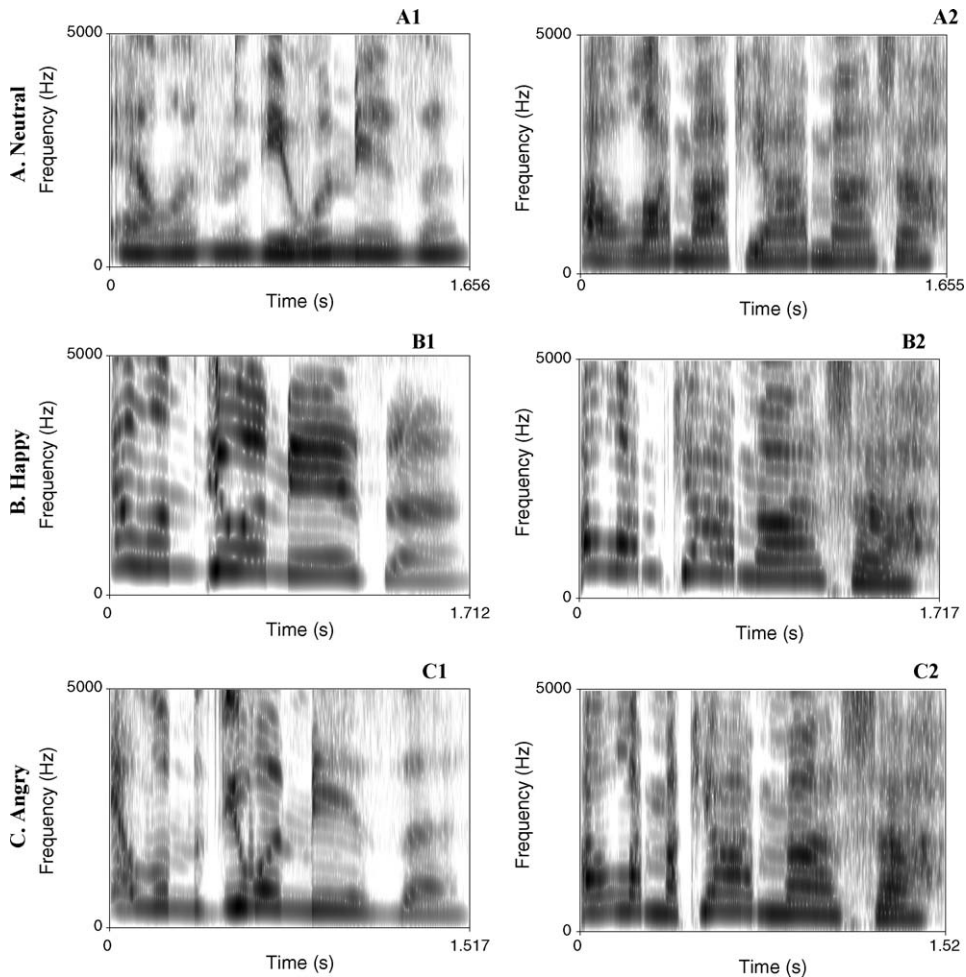
Fig. 1. Examples of sentences' spectograms. This figure shows spectograms for a neutral (A), happy (B), and angry (C) sentence, in the conditions of prosody with semantic content (A1, B1, C1), and 'pure prosody' (A2, B2, C2).
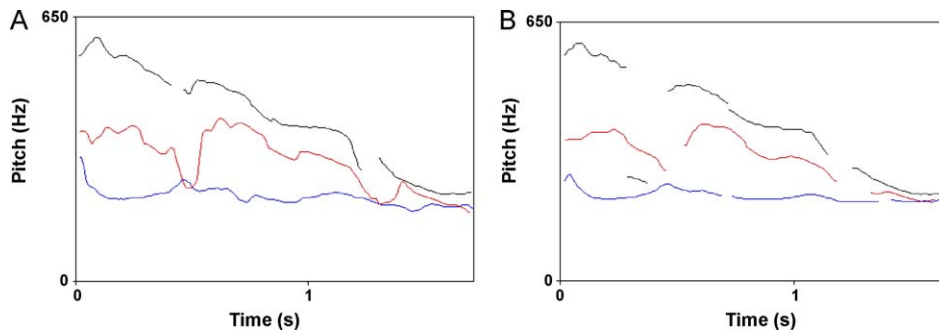
Fig. 2. Shifts in fundamental frequency (F0) for each emotion (happy, angry, and neutral) in both sentence conditions (prosodic sentences with semantic content = A; 'pure prosody' sentences = B). This figure illustrates that sentences' F0 was preserved after transformation for extraction of intelligible semantic content. *Notes*: black = happy; red = angry; blue = neutral. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

2.3. Procedure

Each participant was seated comfortably at a distance of 115 cm from a computer monitor in a sound-attenuating chamber, with a button box in front of them. Sentences were presented binaurally through headphones. Since the second task could be more complex (the sentences were not natural and different from what the participants are used to hear) and because participants could have more difficulties in understanding task instructions, the semantically meaningful sentences were presented first for all participants. Thus, participants listened to 93 intelligible sentences presented in three separate lists, in order to provide a short break during sentences' presentation, minimize participants' fatigue and movements, and maximize their focus on the task. In a second block, they listened to 93 unintelligible sentences, also presented as three separate lists. No sentences were repeated.
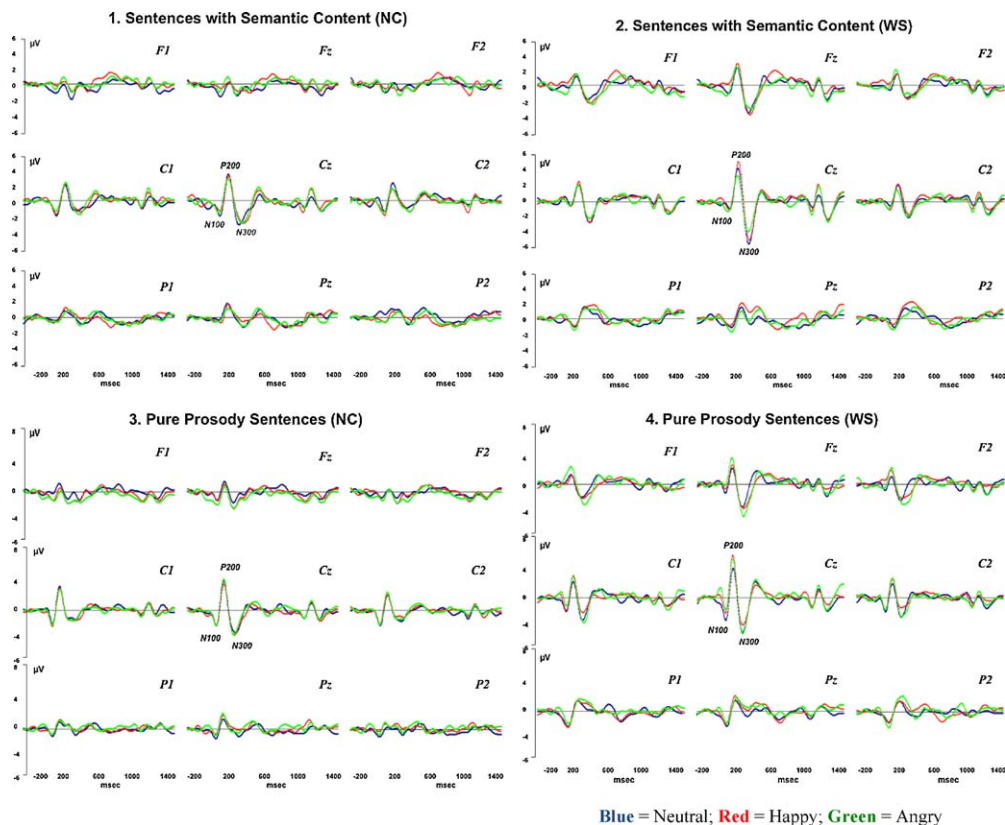
Fig. 3. ERP Grand Averages for Sentences with Semantic Content and Pure Prosody Sentences in TD (1 and 3) and WS (2 and 4) groups. Frontal, central, and parietal electrodes are shown. The maximal effects were observed for central and frontal electrodes. Three main peaks were modulated by the emotional content of auditory sentences and by the presence or absence of intelligible semantic information: N100, P200, and N300. *Note.* WS group: *N* = 9; TD group: *N* = 10. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Before the experimental session, participants were given a brief training with feedback using 15 sentences (5 neutral, 5 happy and 5 angry), in order to ensure that they were properly differentiating emotional intonations. Participants were instructed to decide whether each sentence was spoken in a neutral, positive or negative intonation, pressing a response key (after the presentation of a visual clue – a question mark) with a picture of a cartoon of emotion in order to minimise working memory demands. The order of buttons for each response was counterbalanced across participants.

The average sentence length was 1.890 ms. Each trial started with a cue (2000 ms) consisting of a visual icon that warned participants that the sentence was about to begin. After a sentence's presentation, an inter-stimulus interval of 3000 ms followed in order to avoid contamination of ERP response from any motor response. After that, participants saw a question mark (1000 ms) and then a cartoon reminding them to press a response button presented for a maximum of 4000 ms. As soon as participants gave a response, the next trial started.

2.4. Data acquisition analysis

2.4.1. EEG data recording

While the participants listened to the sentences, the electroencephalogram (EEG) was recorded using QuickAmp EEG recording system (Brain Products, Munich, Germany) with 22 Ag-AgCl electrodes mounted in an elastic cap (Easy Cap), according to the 10–20 System, using an average reference. Electrodes were placed at Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T7, T8, Pz, P3, P4, P7, P8, Oz, O1, O2. Electrode impedance was kept below 5 kΩ. The electrooculogram (EOG) was recorded from electrodes placed at the outer canthus of each eye and from sites below and above the right eye. A ground electrode was placed at Fpz. The EEG signal was recorded continuously and digitized at 250 Hz. Participants were asked to avoid eye and head movements during sentences presentation.

2.4.2. EEG data analysis

The EEG data were analysed using the software package Brain Analyzer (Brain Products, Munich, Germany). EEG epochs containing eye blinks or movement artefacts exceeding $\pm 100 \,\mu V$ were removed from individual ERP averages. After artifact rejection, at least 75% of trials per condition per subject entered the analyses. Following Paulmann and Kotz (2008b) study of prosody processing using non-spliced sentences, individual averages were constructed to the onset of the sentence. Averages were computed using a 200-ms prestimulus baseline and 1500 ms after the onset of the sentence. Due to excessive artifacts, data from two typically developing controls and three WS individuals were not included in statistical analyses or grand averages.

After the inspection of grand averages, three peaks were selected for analysis: N100, P200 and N300. This is consistent with Paulmann and Kotz (2008b), who reported that main effects associated with prosody processing are at the onset of the epoch, and also with the spectogram analysis (see Fig. 2) showing that these effects coincide with major prosodic shifts occurring at the onset of the sentence.

Since peaks were occurring at different times for prosodic sentences with and without semantic content, different latency windows were selected for peak measurement in each sentence condition. N100 was measured as the most negative data point between 100 and 200 ms post-stimulus, for sentences with semantic content; and between 100 and 160 ms post-stimulus for pure prosody sentences. P200 was measured as the most positive data point between 200 and 320 ms post-stimulus for sentences with semantic content; and between 160 and 260 ms for pure prosody sentences. N300 was measured as the most negative data point between 320 and 450 ms post-stimulus for sentences with semantic content; and between 280 and 380 ms for pure prosody sentences.

2.4.3. Statistical analyses

The number of correct responses to the experimental task was analyzed with repeated measures analyses of variance (ANOVA), with sentence condition (prosodic sentences with semantic content vs. 'pure prosody' sentences) and emotionality (neutral, angry, happy) as within-subjects factors, and group (individuals with WS vs. typically developing controls – TD) as between-subjects factor. Reaction time data were not analyzed, because a delay was introduced between the end of the auditory sentence and the response, as described in the previous section.

Visual inspection of grand averages waveforms showed that distribution of ERP effects was predominantly fronto-central. Therefore, electrodes were grouped into two different regions – frontal (Fz, F3, F4), and central (Cz, C3, C4).

Peak amplitude analyses were conducted for each of the selected peaks: N100, P200, and N300. To address the hypotheses of differential processing of emotional and neutral prosody, and of differences in processing prosody with and without semantic content, as indexed by ERP components, repeated measures ANOVAs were calculated with group as between-subjects factor and sentence condition (prosodic sentences with semantic content vs. 'pure prosody' sentences), emotionality (neutral, happy, angry), region (frontal, central), and electrodes (Fz, F3, F4; Cz, C3, C4) as within-subjects factors. In addition, to test for hemispheric differences, additional ANOVAs were computed, with sentence condition (prosodic sentences with semantic content vs. 'pure prosody' sentences), emotionality (neutral, happy, angry), hemisphere (left, right), and electrodes (F3, C3; F4, C4) as within-subjects factors, adding group as between-subjects factor.

For peak latency of the three components of interest (N100, P200 and N300), statistical analyses followed the same ANOVA design as presented for ERP amplitude.

The Geisser-Greenhouse correction (Geisser & Greenhouse, 1959) was applied to all repeated-measures with greater than one degree of freedom in the numerator. Significant interactions were followed by pairwise comparisons, with Bonferroni

Table 4
Mean number of correct responses in WS ($N = 12$) and TD ($N = 12$) groups.

Sentence condition	Emotion	Group	Mean (SD)
Prosodic Sentences with Semantic Content	*Neutral*	WS	24.13 (10.71)
		TD	26.75 (7.09)
	Happy	WS	26.88 (7.04)
		TD	27.38 (7.15)
	Angry	WS	20.88 (7.61)
		TD	27.25 (6.09)
Pure Prosody Sentences	*Neutral*	WS	21.50 (9.27)
		TD	26.75 (5.26)
	Happy	WS	21.71 (10.03)
		TD	22.00 (7.47)
	Angry	WS	14.17 (8.95)
		TD	19.78 (6.78)

correction. In addition, when appropriate, post-hoc tests included additional ANOVAs to find the source of significant interactions.

3. Results

3.1. Behavioral results

A significant effect of sentence condition ($F(1, 22) = 19.88$, $p = .000$) was observed: more correct responses were found for sentences with semantic content relative to pure prosody sentences. Also, a main effect of emotion ($F(2, 44) = 12.58$, $p = .000$) was observed, with angry sentences being associated with more errors relative to happy and neutral sentences. In addition, results showed a significant sentence condition × emotion interaction ($F(2, 44) = 7.33$, $p = .003$). A difference between sentence conditions was observed only for happy and angry prosody, with more errors found in the pure prosody condition.

There were no significant differences between groups in the accuracy of emotional prosody discrimination ($p > .05$), although the TD group showed somewhat higher number of correct responses (see Table 4). However, a significant group × emotion type interaction ($F(2, 44) = 3.42$, $p = .044$) revealed that participants with WS showed more errors than TD controls for angry sentences.

3.2. ERP results

Figs. 3 and 4 illustrate Grand Average waveforms for WS and TD groups, showing a negativity around 100 ms post-stimulus onset (N100), followed by P200 and N300.

Below, we discuss the significant main effects and interactions for each component for each electrode region of interest. We have divided the description of the results into those that were observed in both groups (General prosody effects) and those that pointed to group differences – WS group vs. TD group – in the processing of prosody (Group prosody effects).

In order to control for chronological age and IQ effects, a multivariate general linear model was used, adding chronological age and IQ as covariates. No significant effects of chronological age were found for N100 ($F(1, 15) = 1.886$, $p = .522$), P200 ($F(1, 15) = 3.515$, $p = .398$), or N300 ($F(1, 15) = 1.790$, $p = .534$). Also, no main effects of IQ were found for any of the analyzed components: N100, ($F(1, 15) = 0.776$, $p = .726$), P200 ($F(1, 15) = 0.844$, $p = .706$), and N300 ($F(1, 15) = 43.925$, $p = .118$).

3.2.1. Amplitude

3.2.1.1. N100. General prosody effects. A significant effect of sentence condition ($F(1, 17) = 14.378$, $p = .001$), and region ($F(1, 17) = 11.924$, $p = .003$) was found. N100 amplitudes were more negative for pure prosody sentences relative to sentences with semantic content ($p = .001$), and more negative at central relative to frontal electrodes ($p = .003$). The following significant interactions were also observed: sentence condition × region ($F(1, 17) = 6.115$, $p = .024$), and emotion × region ($F(2, 16) = 4.111$, $p = .036$). Pairwise comparisons showed that, at central ($p = .001$) but not at frontal ($p = .093$) electrodes, significantly more negative amplitudes were observed for 'pure prosody' sentences relative to sentences with semantic content. Also, a region difference in N100 amplitude was found for neutral ($p = .003$) and happy ($p = .001$) intonations: N100 amplitude was more negative at central than at frontal electrodes. No hemispheric differences were observed ($F(1, 17) = 0.892$, $p = .358$).

Group prosody effects. No main effect of group was observed when computing an omnibus ANOVA with sentence condition, emotion, region and electrodes as within-subjects factors ($F(1, 17) = 0.919$, $p = .351$). However, the interaction between sentence condition, emotion, and group approached significance ($F(2, 16) = 2.712$, $p = .097$), as well as the interaction between sentence condition, region, and group ($F(1, 17) = 3.806$, $p = .068$). Pairwise comparisons showed a trend for group differences for happy sentences with intelligible semantic content ($p = .082$): typically developing controls tended to show more negative N100 amplitude relative to WS individuals. Also, a group difference ($p = .049$) was observed for
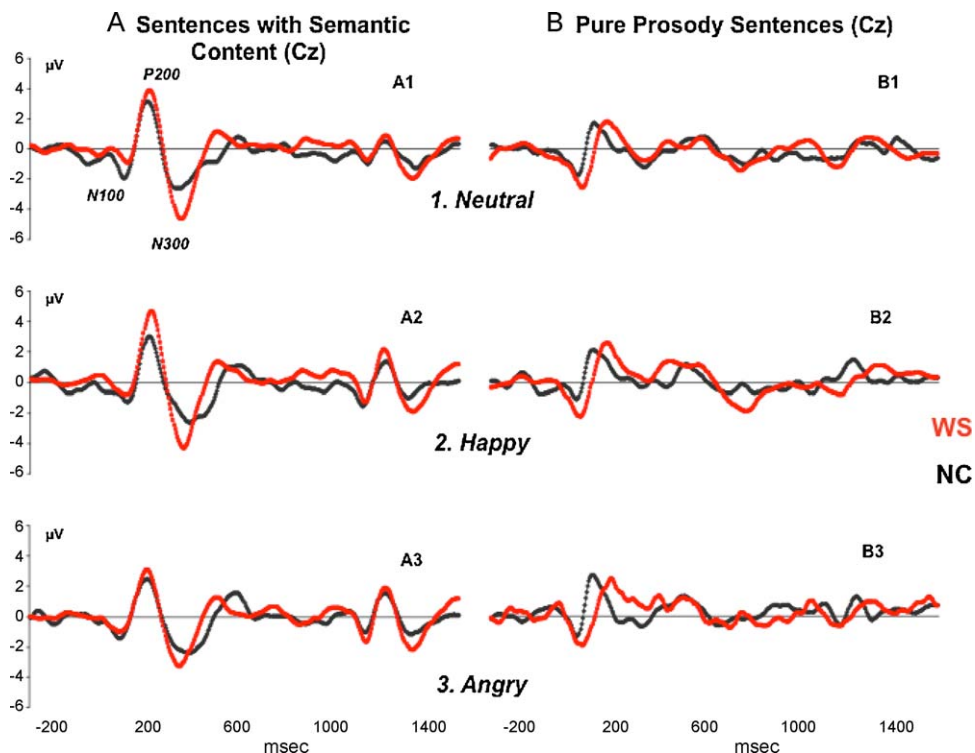
Fig. 4. ERP Grand Averages at Cz. Group contrasts are shown for each prosody type (1 – neutral, 2 – happy, and 3 – angry) in each sentence condition – prosodic sentences with semantic content (A), and pure prosody sentences (B). *Note.* WS group: $N = 9$; TD group: $N = 10$.

sentences with semantic content at central electrodes: more negative N100 was found again in TD controls relative to WS individuals.

3.2.1.2. P200. General prosody effects. Significant effects of sentence condition ($F(1, 17) = 12.938$, $p = .002$), and region ($F(1, 17) = 33.725$, $p = .000$) were observed. Pairwise comparisons revealed that P200 amplitude was more positive for pure prosody sentences relative to sentences with semantic content ($p = .002$) and, in addition, that more positive amplitudes were observed at central electrodes, relative to frontal electrode sites ($p = .000$).

No significant main effect of hemisphere was observed ($F(1, 17) = 1.725$, $p = .207$). However, results showed a trend for an interaction between sentence condition, emotion, and hemisphere ($F(2, 16) = 2.719$, $p = .096$). Pairwise comparisons showed that, for neutral sentences in the 'pure prosody' condition, there was a difference between hemispheres ($p = .044$), with P200 amplitude being more positive in the left hemisphere.

Group prosody effects. For the omnibus ANOVA with sentence condition, emotion, region and electrodes as within-subjects factors, a main effect of group ($F(1, 17) = 4.057$, $p = .060$) approached significance, suggesting a trend for more positive amplitudes in the WS group across sentence conditions and emotional prosody types.

A significant interaction between group, sentence condition, and emotion was observed ($F(2, 16) = 3.879$, $p = .042$). Given the significance of P200 during the early discrimination of neutral and emotional prosody (Paulmann & Kotz, 2008b), we followed this interaction with separate analysis for each condition, with within-subjects factors of emotion, region, and electrodes as described above. A main effect of group was observed for sentences with semantic content ($F(1, 17) = 5.746$, $p = .028$), with more positive P200 in the WS group relative to controls, but not for 'pure prosody' sentences ($F(1, 17) = 2.118$, $p = .164$).

In addition, we conducted separate ANOVAs for each prosody type (neutral, happy, and angry), with sentence condition, region, and electrodes as within-subjects factors. We found a main effect of group for happy sentences ($F(1, 17) = 5.849$, $p = .027$), with more positive amplitudes observed in the WS ($M = 2.977$; $SD = 0.341$) relative to the control group ($M = 1.833$; $SD = 0.326$), consistent with reports of greater sensitivity of WS to happy intonations. In addition, group differences was also observed for angry prosody ($F(1, 17) = 4.370$, $p = .052$): again, more positive P200 amplitude were found in WS ($M = 2.750$; $SD = 0.326$) relative to TD group ($M = 1.810$; $SD = 0.310$).

3.2.1.3. N300. General prosody effects. A significant effect of sentence condition ($F(1, 17) = 18.838$, $p = .000$) was found. More negative N300 was found for pure prosody relative to semantic prosody sentences. A main effect of hemisphere was also observed ($F(1, 17) = 6.755$, $p = .019$): more negative N300 was observed in electrodes of the left relative to the right hemisphere.

Group prosody effects. Within the P300 time window, a main effect of group approached significance ($F(1, 17) = 3.788$, $p = .068$): more negative N300 amplitude tended to be found in the WS group relative to TD controls. In addition, a significant

sentence condition × electrodes × group interaction was found ($F(2, 16) = 3.547$, $p = .053$). Planned pairwise comparisons revealed that, for sentences with semantic content, group differences (more negative N300 for WS relative to TD group) were observed at Fz ($p = .025$).

In addition, an interaction between sentence condition, hemisphere, and group was found ($F(1, 17) = 5.259$, $p = .035$): pairwise comparisons showed a trend for group differences at electrodes of the right hemisphere, both for sentences with semantic content ($p = .064$) and 'pure prosody' sentences ($p = .057$), in which more negative N300 characterized the WS group relative to controls.

Summary

Consistent with our initial hypothesis based on existing literature, sentences with and without intelligible semantic content were processed differently, as indexed by N100, P200, and N300. The processing of pure prosody sentences was associated with more negative N100, more positive P200, and more negative N300, when compared to sentences with semantic content. For all of the components, the effect was predominantly central. The results also suggest group differences in the processing of both sentence conditions and emotional prosodic intonations. Individuals with WS tended to show reduced N100 for sentences with intelligible semantic content, at central electrodes; more positive P200 amplitude for sentences with semantic content, and, in particular, for happy and angry sentences; and a trend for negative N300 both for sentences with semantic content and 'pure prosody' sentences.

3.2.2. Latency

3.2.2.1. N100

General prosody effects. A significant effect of sentence condition ($F(1, 17) = 27.908$, $p = .000$), and emotion ($F(2, 16) = 4.153$, $p = .035$) was observed (see Table 5). N100 latency peaked earlier to pure prosody sentences ($M = 131.61$ ms; $SD = 3.13$) relative to sentences with semantic content ($M = 157.32$ ms; $SD = 4.70$). Although pairwise comparisons did not reveal significant differences between emotional prosody types, a trend was observed for earlier N100 peak latencies for angry sentences ($M = 138.20$ ms; $SD = 3.99$) relative to neutral ($M = 147.68$ ms; $SD = 3.89$) ($p = .067$) and happy sentences ($M = 147.52$ ms; $SD = 3.79$) ($p = .076$). No main effect of hemisphere was found ($F(1, 17) = 1.011$, $p = .329$). However, the interaction between emotion and hemisphere reached significance ($F(2, 16) = 5.232$, $p = .018$): for neutral sentences, N100 peaked significantly earlier at electrodes of the left relative to the right hemisphere ($p = .003$).

Group prosody effects. A trend for a main effect of group was found ($F(1, 17) = 3.128$, $p = .095$): earlier N100 peak latency was found in WS relative to TD group. Results showed a significant sentence condition × region × group interaction ($F(1, 17) = 4.321$, $p = .053$). Pairwise comparisons showed group differences for 'pure prosody' sentences at frontal electrodes ($p = .007$): N100 peaked earlier in the WS group relative to TD controls.

3.2.2.2. P200

General prosody effects. A significant effect of sentence condition was observed ($F(1, 17) = 476.587$, $p = .000$): P200 peaked earlier to pure prosody sentences relative to sentences with semantic content. In addition, a main effect of hemisphere was found ($F(1, 17) = 5.967$, $p = .026$): N100 peaked earlier at electrodes of the left relative to the right hemisphere.

Group prosody effects. A trend for a main effect of group was found ($F(1, 17) = 3.879$, $p = .065$): P200 tended to peak earlier in WS relative to TD group.

3.2.2.3. N300

Global prosody effects. A main effect of sentence condition was observed ($F(1, 17) = 109.998$, $p = .000$). An earlier N300 peak latency was again observed for pure prosody sentences.

Group prosody effects. No main effect of group or interactions with group factor were observed.

Table 5
Peak latency values (N100, P200, N300), at Cz, for sentences with semantic content and pure prosody sentences.

Peak	Groups	Sentence condition					
		Sentences with Semantic Content, Mean (*SD*)			Pure Prosody Sentences, Mean (*SD*)		
		Neutral	Happy	Angry	Neutral	Happy	Angry
N100	WS	148.00 (38.21)	167.56 (26.72)	147.11 (43.99)	120.44 (32.95)	127.56 (8.82)	127.56 (9.68)
	TD	168.00 (22.07)	149.60 (51.02)	152.80 (20.38)	131.60 (8.10)	130.00 (14.88)	128.40 (10.57)
P200	WS	269.78 (17.10)	277.33 (15.10)	262.67 (19.60)	210.22 (12.98)	209.33 (10.77)	206.67 (12.96)
	TD	267.20 (13.17)	266.80 (15.44)	262.00 (23.34)	213.20 (25.16)	213.60 (25.03)	210.80 (11.93)
N300	WS	395.11 (9.55)	405.33 (21.07)	378.22 (30.40)	320.44 (18.60)	328.89 (31.99)	318.67 (21.35)
	TD	378.80 (27.72)	422.00 (67.84)	396.40 (45.19)	331.20 (39.72)	330.00 (28.86)	325.60 (32.51)

Note. WS group: $N = 9$; TD group: $N = 10$.

Summary

Earlier peak latencies were observed for pure prosody sentences relative to prosodic sentences with semantic content, for all ERP components (N100, P200, and N300).

Marginally significant group differences were observed for peak latency measures for N100 and P200. The WS group tended to show earlier N100 and P200 peak latency. No group differences in peak latency values were observed for the N300.

4. Discussion

The current study explored the following questions: (a) Do WS individuals process emotional prosody differently relative to typically developing individuals at both behavioral and electrophysiological levels? (b) Does the presence of semantic information influence the processing of prosodic information at both behavioral and electrophysiological levels? Previous studies have suggested an extensive use of prosodic devices by individuals with WS, as well as a relative sensitivity to emotional prosody (Plesa-Skwerer et al., 2006), but few studies have investigated WS individuals' ability to identify different prosody patterns and none has investigated the electrophysiological correlates of prosody processing.

Subjects were presented with meaningful, semantically neutral sentences spoken with different emotional intonations, and with the same sentences after they were transformed to eliminate semantic and lexical information. Both behavioral and ERP data were collected. Behavioral data suggested differences between groups in the recognition of negative (angry) prosody, with more errors found in WS. This is consistent with anecdotal reports of WS abnormalities in processing negative social information (Bellugi et al., 2000; Jones et al., 2000; Klein-Tasman & Mervis, 2003). However, these data differ from a previous study (Plesa-Skwerer et al., 2006) reporting better recognition for angry intonation than for other emotions in WS.

In both groups, emotion recognition was better for sentences that contained semantic information than for pure prosody sentences devoid of it (77.29% vs. 61.71% correct for the WS group; 87.52% vs. 73.68% for the TD group), confirming the findings of previous studies that interpreting prosody in the absence of meaningful semantic content is more difficult (Kotz & Paulmann, 2007; Paulmann et al., 2010).

ERP data pointed to important group differences and similarities. In both groups, N100, P200 and N300 amplitudes were larger and their latencies peaked earlier in pure prosody sentences than in sentences with semantic content. This result suggests that, in the absence of intelligible semantic information, the subject has fewer linguistic channels to process, so that the processing of suprasegmental features can be faster.

The WS group showed a similar morphology and sequence of ERP components to typically developing controls. At the same time, group differences were observed in the N100, P200 and N300 components. Relative to controls, individuals with WS tended to show reduced N100 amplitude for sentences with semantic content; more positive P200 amplitude for semantic prosody, specifically for happy and angry intonations; and a trend for more negative N300 for both types of sentence conditions. Also, a trend for group differences in latency was observed for N100 and P200, with peaks tending to occur earlier in the WS group relative to controls.

In the following section, an integrative approach for abnormal electrophysiological correlates of prosody processing in WS is presented, based on Schirmer and Kotz (2006) three stage working model for the processing of emotional prosody.

4.1. N100: sensory processing

The existing evidence suggests that the first stage of emotional prosody processing occurs around 100 ms, when the sensory processing of acoustic cues takes place (Schirmer & Kotz, 2006). Traditionally, the auditory N100 component is associated with the processing of physical characteristics of stimuli, such as intensity (Keidel & Spreng, 1965), sound complexity (Wunderlich & Cone-Wesson, 2001). More recently, it has been proposed to reflect cortical responsiveness to natural speech sounds (Ford & Mathalon, 2004; Ford et al., 2007).

In the current study, N100 amplitude in WS tended to be reduced to sentences with semantic content but not to pure prosody sentences suggesting that early stages of prosody processing are adversely influenced by the processes related to extracting semantic information: WS individuals can process prosodic information effectively if they are unimpeded by additional demands of processing a semantic channel. Thus, for N100, the results are in keeping with the notion that difficulty in prosody processing is conferred by the simultaneous need to process semantic content (Plesa-Skwerer et al., 2006). However, since N100 amplitude is modulated by a long list of variables such as attention, arousal, motivation, fatigue, and hearing thresholds, we cannot rule out a possibility that they may have additionally contributed to the observed results.

4.2. P200: integration of emotionally significant acoustic cues

The second stage of emotional prosody processing, occurring around 200 ms, corresponds to the integration of emotionally significant acoustic cues that allow subjects to derive emotional significance from the stimuli (Schirmer & Kotz, 2006). This is consistent with the functional significance of the auditory P200 component believed to index some aspects of the stimulus classification process (Garcia-Larréa et al., 1992), and to be sensitive to the acoustic properties of stimuli such as

intensity (e.g., Picton et al., 1970), duration (e.g., Roth et al., 1976), and pitch (e.g., Alain, Woods, & Covarrubias, 1997; Jacobson et al., 1992). Variations in these acoustic features (e.g., pitch, intensity) define emotional prosody (see Schirmer & Kotz, 2006). Our findings point to more positive P200 amplitude to sentences with semantic content (in particular to emotional intonations) but not to 'pure prosody' sentences. This finding suggests that the impairment is dependent on the semantic status of the sentences, arguing in favor of a selective role of semantic content as a mediating factor in prosodic abnormalities in WS.

In addition, the finding of enhanced P200 to happy intonation corroborates the findings of an emotional facial expressions processing study (Haas et al., 2009) where a heightened reactivity/attention was observed to positive social cues in WS (larger P300–500 difference to happy minus neutral facial expressions). However, the finding of enhanced P200 to angry intonation is not consistent with the reported decreased activity to fearful vs. neutral expressions (indexed by a reduced N200 mean amplitude for fearful expressions) in the same study, but is in line with the report of aberrant processing of negative human vocalizations (Järvinen-Pasley et al., 2010).

For both happy and angry vocal information, it seems that WS individuals react in an increased way, irrespective of valence, consistent with anedoctal reports of greater sensitivity to emotional prosody in WS (Gonçalves et al., 2004, 2010; Jones et al., 2000; Reilly et al., 1991, 2004).

In spite of a greater sensitivity to emotional cues, as suggested by P200 amplitude for happy and angry intonations, behavioral results indicate higher error rates for angry sentences in WS. Therefore, these results seem to suggest both dysfunctional early perceptual analysis of emotional stimuli and disrupted late evaluation of angry stimuli. In the context of social interactions, deficits in discriminating negative affective states, within the auditory domain, may be related to inappropriate social behavior (e.g., Davies et al., 1998; Gosch & Pankau, 1994; Laws & Bishop, 2004; Udwin & Yule, 1990).

4.3. N300: cognitive evaluation of emotional significance

The N300 has been associated with the cognitive evaluation of emotional significance of the acoustic signal (around 400 ms) related to integrating information provided by the physical properties of the stimuli (as intensity, pitch, duration) and meaning conveyed by linguistic (e.g., semantic) information so that cognitive judgments can be made (e.g., what type of emotion is being presented?) (Schirmer & Kotz, 2006; see also Kotz & Paulmann, 2007; Paulmann & Kotz, 2008b; Wambacq & Jerger, 2004).

The trend for enhanced N300 peak amplitude in individuals in WS for both sentences with semantic content and 'pure prosody' sentences suggests abnormal electrophysiological response at the stage of evaluating emotional significance of the message. This is consistent with previous studies suggesting WS difficulties in discriminating and understanding emotional auditory cues (Catterall et al., 2006; Plesa-Skwerer et al., 2006; Skwerer et al., 2007).

Together, ERP results paint a more nuanced picture of abnormalities in processing prosody in WS due to the ERP sensitivity to processes that are not accessible to behavioral measures. At the level of sensory signal processing, indexed by N100, its reduced amplitude to sentences with semantic content suggests an impairment that is likely mediated by the impact of semantic channel on the efficient processing of prosodic cues. At the level of the integration of specific emotional cues, as indexed by P200, its amplitude enhancement to sentences with semantic content suggests that heightened sensitivity to prosodic cues depends on whether WS individuals need to process semantic information or not. Finally, the trend for increased N300 in WS suggests abnormal processes of cognitive evaluation of emotional significance of the acoustic signal.

We do not believe that these abnormalities stem from WS individuals' inability to retain pitch variations over longer prosodic segments in short-term memory since a relative preservation of phonological short-term memory in WS has been reported (Grant et al., 1997; Majerus et al., 2003; Robinson et al., 2003). Instead, we believe that these results suggest specific impairments in prosody processing that span the three stages: (1) sensory processing of acoustic signal; (2) integration of emotionally specific acoustic cues; and (3) cognitive evaluation of the emotional significance of acoustic cues and its integration with semantic information. The suggestion, from behavioral studies, that individuals with WS use or interpret intonation in a different way from what would be expected for their chronological age is corroborated by ERP findings.

It is worth noting that less negative N100 and more positive P200 amplitudes in WS individuals have already been described in previous studies using normal speech (Mills et al., 2003; Neville et al., 1994; St. George et al., 2000), a finding that was interpreted as indexing the hyperexcitability of the auditory system in WS, and can be related to structural abnormalities in brain areas thought to be the generators of N100, i.e., the superior temporal gyrus (STG). For example, Reiss et al. (2000) reported an increase of STG volume relative to decreased overall brain and cerebral volumes, and the absence of a normal left > right asymmetry was reported by Sampaio et al. (2008).

The major contribution of this study is providing, for the first time, electrophysiological evidence for the abnormalities in emotional prosody processing in WS. However, some limitations should be highlighted. Due to the small sample that participated in this study, the current results should be treated with caution. In addition, the intra-group variability and heterogeneity of WS (e.g., Plesa-Skwerer et al., 2006) that could lead to observing different patterns of prosodic deficit in WS across different samples (Catterall et al., 2006) should be kept in mind. Also, due to small sample size, some main effects and interactions involving group factor were only marginally significant. Therefore, future studies should include larger samples to provide a more comprehensive view of prosody processing in WS.

5. Conclusion

Overall, the findings from the current study suggest that prosody in WS is processed in a different way from typically developing controls, both in terms of different types of emotionality (positive vs. negative vs. neutral), and in terms of the presence or absence of semantic content of a sentence.

Abnormalities indexed by N100, P200 and N300 likely represent deficits in early sensory stages of prosody processing and suggest that dysfunction in the processing of suprasegmental features in WS may not be entirely mediated by higher order cortical deficits such as for example executive functioning (e.g., Greer, Brown, Pai, Choudry, & Klein, 1997; Lincoln, Lai, & Jones, 2002; Morris & Mervis, 2000; see Martens et al., 2008 for a review) or semantic processes (e.g., Bromberg, Ullman, Marcus, Kelly, & Levine, 1995; Temple, Almazan, & Sherwood, 2002; Tyler et al., 1997; Ypsilanti, Grouios, Zikouli, & Hatzinikolaou, 2006; see Brock, 2007 for a review); instead, they also indicate a bottom-up contribution to the impairment in emotional prosody processing and comprehension.

The current study showed, for the first time, that abnormalities in ERP measures of early auditory processing in WS are also present during the processing of emotional vocal information. This may represent a physiological signature of underlying impaired on-line language processing, as proposed for other neurodevelopmental disorders such as schizophrenia (e.g., Rosburg et al., 2008). Given that during speech perception, both segmental and suprasegmental information closely interact (e.g., Dietrich, Ackermann, Szameitat, & Alter, 2006; Schirmer & Kotz, 2006), deficits in understanding the "emotional melody" of discourse will compromise the ability to understand the intentions and affective states of the speaker in WS. This suggests that clinical interventions with WS individuals should include strategies for training the ability to differentiate emotional prosodic intonations.

Acknowledgements

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