Journal of Autism and Developmental Disorders
https://doi.org/10.1007/s10803-019-04040-x

ORIGINAL PAPER

A Spectrotemporal Correlate of Language Impairment in Autism Spectrum Disorder

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Abstract
This study introduces an objective neurophysiological marker of language ability, the integral of event-related desynchronization in the 5–20 Hz band during 0.2–1 seconds post auditory stimulation with interleaved word/non-word tokens. This measure correlates with clinical assessment of language function in both ASD and neurotypical pediatric populations. The measure does not appear related to general cognitive ability nor autism symptom severity (beyond degree of language impairment). We suggest that this oscillatory brain activity indexes lexical search and thus increases with increased search in the mental lexicon. While specificity for language impairment in ASD remains to be determined, such an objective index has potential utility in low functioning individuals with ASD and young children during language acquisition.

Keywords Language impairment · Oscillation · Lexical access · Magnetoencephalography (MEG)

Autism spectrum disorder (ASD) represents a highly prevalent (1 in 59 children; Baio et al. 2018) neurodevelopmental disorder with a heterogeneous constellation of phenotypic characteristics. In part because of this heterogeneity, progress in unraveling the neural signatures associated with ASD has been hampered. Approaches that recognize individual differences in aspects of the phenotype and use domain-specific dimensional correlates *across* the spectrum offer a promising avenue to appreciate both generalizable and specific (individual) features. While no longer considered a core symptom of ASD (American Psychiatric Association 2013), language impairment remains a common feature of ASD presentations (Mody and Belliveau 2013). In fact up to 30% of children with ASD are minimally verbal (Tager-Flusberg and Kasari 2013), with widely varying degrees of language compromise in the remaining population (Tager-Flusberg et al. 2001). While verbal ability is highly variable within the ASD population, ranging from minimally verbal subjects to those with above normal verbal intelligence quotients, deficits in pragmatic language are nearly universal (Volden et al. 2009; Young et al. 2005).

Electrophysiological techniques such as electroencephalography (EEG) and magnetoencephalography (MEG) have been applied to studies of auditory processing in children and adolescents with ASD. Many of these studies have focused on identifying sensory processing anomalies in the auditory response to simple stimuli, such as tones, clicks, or vowel sounds, relative to typically developing (TD) peers (Kikuchi et al. 2016). Specifically, delays in prominent middle and late latency components (M50, M100) of the auditory evoked field (Gage et al. 2003; Oram Cardy et al. 2004; Roberts et al. 2010; Yoshimura et al. 2013) and to components of the auditory mismatch field (Matsuzaki et al. 2017; Roberts et al. 2011; Schwartz et al. 2018) have been observed. Similarly, there is evidence of altered oscillatory activity of the auditory cortex in ASD. Reduced post-stimulus gamma-band activity (> 30 Hz) has reliably been observed in children and adults with ASD (Edgar et al. 2015; Port et al. 2016; Wilson et al. 2007) and in 1st degree relatives (McFadden et al. 2012; Rojas et al. 2011). It is notable that despite ASD-associated findings of alterations in these auditory processes, correlations with language ability have been mostly elusive and, if at all, have best been demonstrated in paradigms using speech elements (Oram Cardy et al. 2008; Roberts et al. 2011; Yoshimura et al. 2013) or investigating

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Published online: 08 May 2019

oscillatory responses to word stimuli (McFadden et al. 2012).

In non-patient populations, components of the late-field evoked response (i.e. using stimulus-locked time domain averaging) have shown to be sensitive to lexical processing (Embick et al. 2001; Pylkkanen and Marantz 2003; Pylkkanen et al. 2002). An alternative approach focuses on assessing task-related changes in oscillatory activity at different frequencies and times (Bastiaansen et al. 2012). One way to quantify these effects is to measure relative increases (event related synchrony: ERS) and decreases (event related desynchrony: ERD) in the power of specific frequency bands following a stimulus. Prior studies have shown that ERD/ERS in the theta (4–6 Hz), alpha (8–12 Hz) and beta (13–30 Hz) in the post stimulus late-field (post 200 ms) are sensitive to language-related processes in superior temporal gyrus (Brennan et al. 2014; McFadden et al. 2012; Tavabi et al. 2011). These findings are in accord with prior EEG studies that have observed ERD/ERS in the theta, alpha and beta bands in response to written word-class stimuli (Bastiaansen et al. 2005, 2008). Studies using auditory memory tasks (words and vowels) in children and adults have also shown ERD/ERS in these frequency bands, identifying in particular alpha ERD responses during auditory recognition of target words (Krause et al. 2007; Pesonen et al. 2006).

In this study we focus on the oscillatory response of the auditory cortex to basic lexical information using an interleaved word/non-word paradigm. Specifically, we examine the relationship between measures of language function and the integral of event related desynchronization between 5 and 20 Hz (theta—low beta band) in the late fields following stimulus tokens in a word/non-word interleaved paradigm. Our study addresses the following questions: (1) *would the integral of such 5–20 Hz event-related synchronization index language ability across a range of language impairment and typical language functioning*? and (2) *would there be an additional influence of ASD on ERD integral, either a deficit compared to typically-developing controls, or evidence of compensatory hyper-activity compared to language ability-matched peers?* The ability to assess the neural correlates of elements of language processing would potentially yield insight into the spectrotemporal dynamics of language processing in the brain, identifying anomalous processing patterns indicative of language impairment as well as potentially revealing compensatory mechanisms in ASD individuals with preserved language ability. In part because of the passive design, this approach, once validated, also offers the potential to study extreme language impairment in low functioning individuals with ASD, as well as in younger children and infants during language acquisition and development.

Methods

Participants

Seventy children (51 with ASD, 19 TD) between the ages of 6 and 10.9 years of age were enrolled into the study. For each participant, ASD diagnosis was confirmed by a licensed child psychologist, using the Autism Diagnostic Observation Schedule (ADOS-2; Lord et al. 2012), the parent report on the Social Communication Questionnaire (SCQ; Rutter et al. 2003) and the parent report of the Social Responsiveness Scale (SRS-2; Constantino and Gruber 2012). For any child for whom a diagnostic discordance existed (e.g. a child who exceeded ADOS diagnostic cut-offs but was below SCQ and SRS cut-offs), the parent-completed Autism Diagnostic Interview-Revised (ADI-R; Rutter et al. 2003) was used to resolve the discordance. It should be noted that in the final ASD cohort the ADI-R was used in only 3 cases. ASD symptom severity was measured using the ADOS calibrated severity score (ADOS-CSS; Gotham et al. 2009). To rule out global cognitive delay, subjects with a Perceptual Reasoning Index (PRI) score below 70 on the Wechsler Intelligence Scale for Children-IV (WISC-IV; Wechsler 2003) were excluded. Similarly, TD subjects were excluded based on a prior diagnosis (per parent report screening questionnaire) of any of the following: learning disability, intellectual disability, communication disorder or psychiatric conditions including bipolar disorder, obsessive compulsive disorder, schizophrenia, conduct disorder, depression or anxiety disorder. Language understanding and expression was evaluated using the Core Language Standard Score (CELF-CLSS) from the Clinical Evaluation of Language Fundamentals (CELF-4; Semel et al. 2003).

From the 51 ASD participants, three were unable to complete the imaging protocol (one MEG, two MRI) and, due to excessive motion or artifacts, an additional seven did not have evaluable data (four MEG, three MRI). An additional six ASD participants were excluded because despite a community diagnosis, they did not meet diagnostic criteria when observed by the study psychologist. Similarly, four TD participants were excluded, as one participant did not complete the MEG protocol, and three did not have evaluable data (one MEG, two MRI) due to excessive artifacts. Therefore, the evaluable sample for this study included 35 children (31 male, four female) with ASD (mean ± standard deviation: 9.4 ± 1.1 years) and 15 (12 male, three female) TD children (age 8.8 ± 1.4 years). Ages were not significantly different ($p = 0.145$). The gender balance in the final evaluable sample also was not significantly different between groups (Chi square test: $p = 0.423$). As expected, groups significantly differed

($p < 0.001$) on measures of ASD symptomatology: SCQ, SRS Total t-score, ADOS-Total and ADOS-CSS. Please refer to Table 1 for group means and standard deviations. Groups also differed significantly on language ability measured via CELF-CSS (TD: 114.8 ± 8.0; ASD: 89.1 ± 26.2; $p < 0.001$) and differed marginally on nonverbal cognitive ability measured by PRI (TD: 115.9 ± 16.3; ASD: 105.5 ± 17.8; $p = 0.054$). Within the ASD cohort, 21 participants exhibited symptoms of one or more additional non-ASD diagnosis. 17 participants exhibited symptoms of attention-deficit/hyperactivity disorder, five of anxiety disorder, one of mood disorder and one of developmental coordination disorder.

Demographic parameters for the evaluable sample are listed in Table 1.

The study was approved by the local Institutional Review Board. Written informed consent was obtained from all participant's families and each participant (when competent to do so) gave verbal assent to participate in the study.

Stimuli

Stimuli for this experiment consisted of words and plausible, pronounceable non-words. Word and non-word tokens were selected from the same stimuli database used and fully described in Brennan et al. (2014). Briefly, words were selected to be monosyllabic concrete nouns applicable for use with children (aged 6–10 years): they had a forward association greater than 0.23 (Nelson et al. 1998), log spoken frequency greater than 2.75 (Balota et al. 2007), concreteness greater than 4.5 (Wilson 1988) and age of acquisition less than 6 years (Gilhooly and Logie 1980). No homonyms, homographs or homophones were included in the word stimuli. Pronounceable non-words were formed by changing one, or in a few cases two, phonemes (e.g. "block" → "blick"). All tokens were recorded by a female speaker in a sound-attenuated booth spoken within a carrier phrase ("Say ___ again"), and digitized at 44,100 Hz. As part of a separate experiment, subjects were also presented with temporally modified words. These tokens were generated by changing the sampling frequency by 80% and 120% (35,280 Hz and 52,920 Hz). Data from these tokens were not analyzed as part of the current lexicality experiment but will instead be presented in a subsequent publication. Although these stimuli were word-like, being derived from words, they were neither true "words" nor "non-words" and so were not included in the present analysis. Of note, because of the sparseness of potential word-root repetition, and because of implicit acoustic differences between modified words and their source tokens, little inadvertent priming was anticipated. All stimuli were re-sampled to 22,050 Hz, trimmed to ensure that onsets were precisely aligned across stimuli, and normalized to 70 dB in Praat software (Boersma and Van Heuven 2001).

Table 1 Demographics

	TD (N = 15)		ASD (N = 35)		*p* value
	Mean	SD	Mean	SD	
Age	8.8	1.4	9.4	1.1	0.145
Gender ratio (M:F)	4 (12 M:3F)		7.75 (31 M:4F)		0.429
PRI	115.9	16.3	105.5	17.8	0.054
CELF-CLSS	114.8	8.0	89.1	26.2	<0.001
ADOS-Total	2.0	2.0	10.5	4.4	<0.001
ADOS-CSS	1.5	1.1	6.2	2.3	<0.001
SCQ	3.5	2.8	18.9	6.5	<0.001
SRS total T-score	42.6	5.8	76.8	15.7	<0.001

Procedures and MEG acquisition

Participants were seated in a dimly lit magnetically-shielded room for MEG recording while auditory stimuli were delivered binaurally via transducers and insert-earphones (ER3A, Etymotic Inc.). Auditory tokens were presented with a random inter-trial interval (ITI) ranging from 5.0 to 5.2 s. Stimuli from each class were randomly presented in an interleaved manner for a total scan time of 1320 s (22 min). As stimuli were chosen at random; the ratio of words/non-words varied slightly between participants. On average, slightly more words (53.2 ± 5.7) than non-words (50.5 ± 5.8) were presented ($p = 0.02$). There was no group difference ($p = 0.87$) in the word to non-word ratio. The mean duration of each stimulus was 497 ± 5 ms. There was thus a mean inter-stimulus interval (ISI) of 4.6 s to minimize any potential interaction between stimuli, as responses returned to baseline within ~ 1.5 s (see Fig. 1), allowing for an extended baseline period without wrap-around response contamination. Prior to recording, each participant's hearing threshold was assessed using 1 kHz tones (300 ms duration). Experimental stimuli were presented at 45 dB above threshold (45 dB SL).

Participants were fitted with three fiducial coils, two placed anterior to the left and right tragus of the ear, and one placed on the nasion. These were used to continuously monitor head position during recording and for subsequent co-registration between the MEG data and anatomical images. Electrodes were also placed above and below the left eye to monitor eye-blinks and on the left and right clavicle to monitor the heartbeat. MEG was recorded using 275 CTF axial gradiometers (VSM MedTech, Coquitlam, BC) with third-order synthetic gradiometer noise correction at 1200 Hz.

Structural MRIs were recorded from each participant with a 3T Siemens (Erlangen, Germany) Magnetom Verio

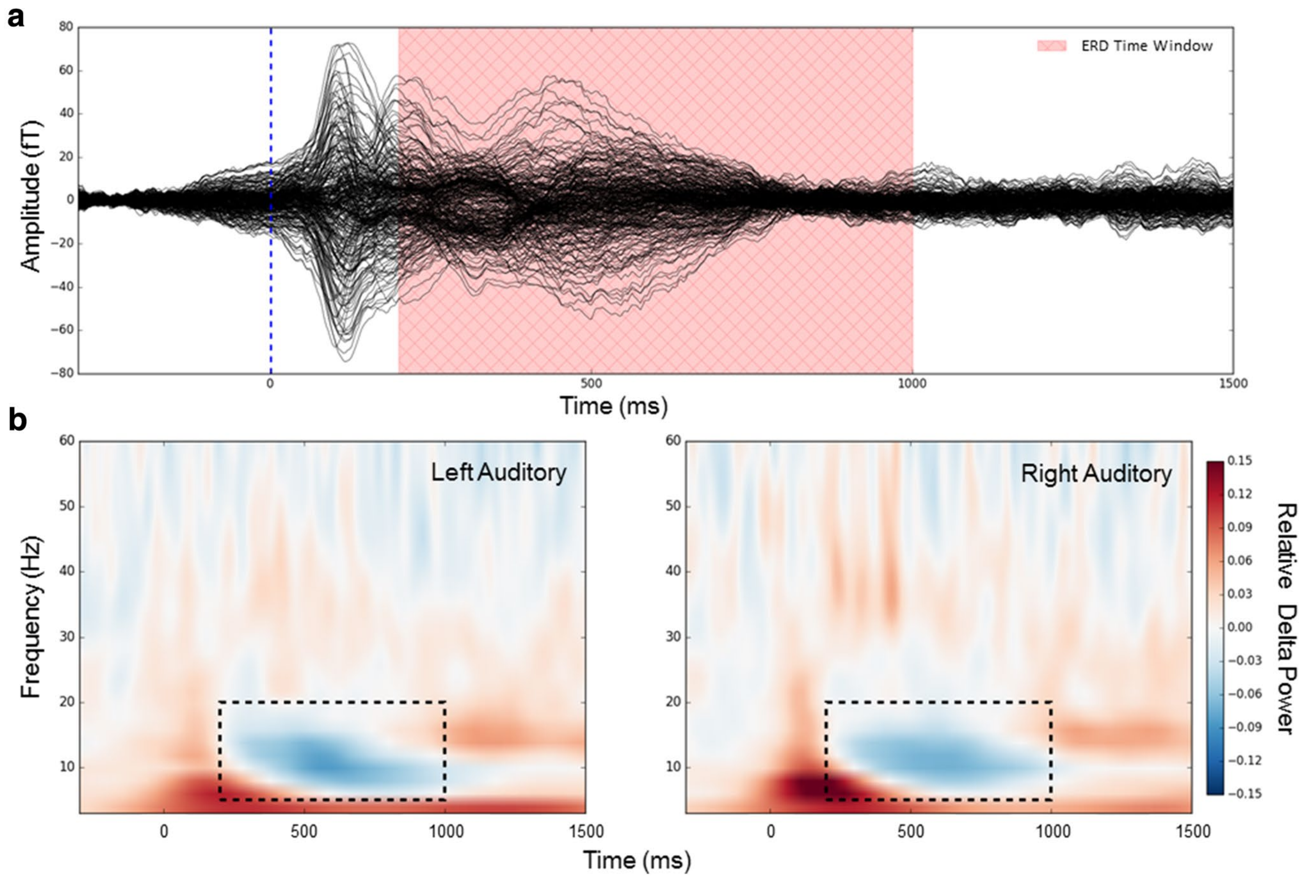

Fig. 1 **a** Sensor waveforms grand-averaged across subject and token, time-locked to token onset. Shaded area (red) indicates the time window used in ERD measurements. **b** Grand average spectro-temporal plots (TFR's) for the left and right auditory cortex source locations

scanner using a 32 channel receive-only head RF coil. We recorded a T1-weighted image for each participant with a magnetization-prepared pulse sequence (MPRAGE) with the following parameters: 126 slices, 1 × 1 × 1 mm voxels, field of view 256, matrix 256 × 256, echo time 2.87 ms, repetition time 1900 ms, flip angle 9°, inversion time 1050 ms.

Data Processing

MEG data was analyzed using the mne-python analysis toolbox (Gramfort et al. 2014). For each dataset, bad channels were detected using the FASTER (Nolan et al. 2010) algorithm to identify channels with high (> 3 *SD*) levels of variance, kurtosis etc. A 60 Hz notch filter and 1–100 Hz bandpass filter were applied to the sensor waveforms. Heartbeat and eye-blink artifacts were identified using independent component analysis (ICA). The data were then epoched − 2 to 2 s relative to the token onset and downsampled to 300 Hz; finally, artifact ICA components were removed from stimulus locked epoched data (See Fig. 1).

Subject-specific single shell head models were created from each participant's MRI data. Freesurfer (Fischl 2012) watershed segmentation was used to identify inner skull surface and a single shell boundary element model (BEM) forward model was computed. MRI to MEG coregistration was achieved using three fiducial points, and further refined using an iterative closest point registration to align the digitized head shape points and the subject's outer scalp surface as defined by MRI.

Separately, right and left auditory cortex source locations (ACtR and ACtL) as well as the left/right frontal lobe, left/right parietal lobe, and five mid sagittal locations (See Fig. 2) were defined on the MNI 152 atlas. Non-auditory sources were included in source modeling to account for activity occurring throughout the brain and to mitigate any potential for non-auditory activity to contaminate auditory waveforms. Source locations were mapped to each participant using non-linear registration of subject MRI data to the MNI152 template using the ANTs (Avants et al. 2011) registration toolkit.

Source waveforms were computed using the minimum norm estimate (Hämäläinen and Ilmoniemi 1994). Total power time–frequency responses (TFRs) were computed separately for right and left auditory sources, using Morlet

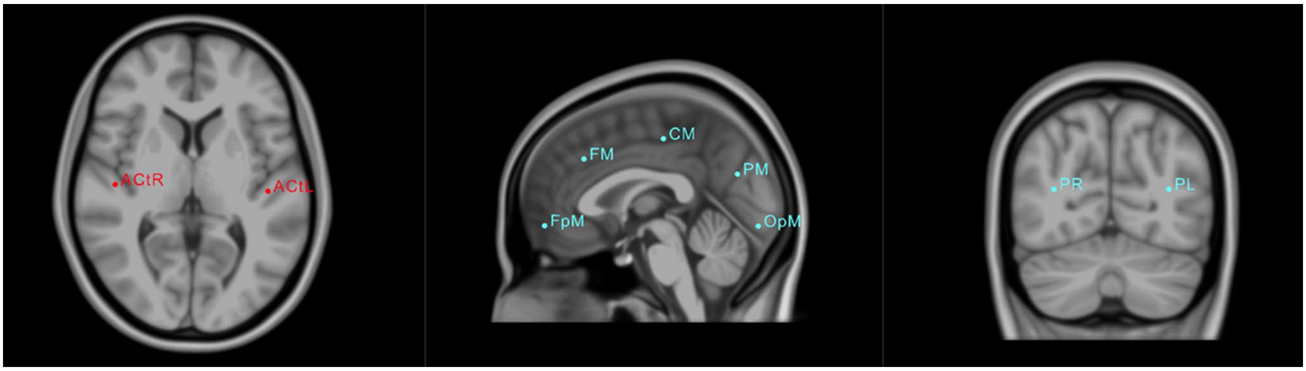

Fig. 2 Left and Right Auditory cortex (ACtL, ACtR) source locations defined on the MNI 152 Atlas. Nine other dipoles are distributed throughout the brain in order to model residual activity

wavelets (7 cycles per frequency) from 3 to 100 Hz in 2 Hz increments (Gröchenig 2013) for each trial, and then averaged by stimuli class (word/non-word). Relative change in total power was calculated per frequency bin relative to a baseline of −2.0 s to −0.2 s prior to the token onset. From each subject's TFR the event related desynchrony (decreased power relative to baseline) was summed between 5 and 20 Hz and 0.2–1.0 s post onset to yield a summary ERD measure per subject. This temporal and frequency range was chosen based on prior MEG studies of single word presentation (Brennan et al. 2014; Tavabi et al. 2011) and confirmed as capturing the spectrotemporal extent of the desynchronization based on grand averaged TFRs (see Fig. 1).

To examine the factors contributing to the ERD integral, we utilized linear mixed models (LMMs) with fixed effects of diagnosis (TD/ASD), hemisphere (ACtL/ACtR) and token (word/non-word) with covariates of age and CELF core language index. Given the repeated observations in each subject (hemisphere and token), we considered subject as a random effect.

We subsequently performed hierarchical regression to identify any possible influence of non-verbal IQ (PRI) or autism severity (indexed by ADOS-CSS) on association with CELF core language index within the ASD cohort. For this, we averaged ERD integral measures across token and hemisphere, because there was no main effect of these factors in the linear mixed model analysis.

Results

The linear mixed effects model with fixed effects of ASD diagnosis, language ability (CELF-CLSS), hemisphere (left/right auditory cortex), token (word/non-word) and age and with subject entered as a random effect, was fit to the summary ERD measure. A significant relationship between ERD and CELF-CLSS was observed (slope: 0.95 ± 0.42; F ratio: 5.17; DF: 46; $p = 0.028$) indicating that greater ERD was associated with better language performance. No significant effects of diagnosis (ASD: 127.63 ± 11.54 vs TD: 99.87 ± 18.77, F ratio: 1.41; DF: 46; $p = 0.242$), age (slope: -0.137 ± 0.68 per month; F ratio: 0.04; DF: 46; $p = 0.84$), token (word: 113.25 ± 10.8 vs. non-word: 114.25 ± 10.8; F ratio 0.02; DF: 148; $p = 0.88$) or source hemisphere (ACtL: 110.5 ± 10.8 vs ACtR: 117.0 ± 10.8; F ratio: 0.91; DF: 148: $p = 0.34$) on ERD were observed. For visualization purposes ERD values were corrected for age (to cohort mean 9.25 years) and averaged across token and hemisphere. Figure 3a shows a scatter plot of age/token/hemisphere-corrected ERD versus CELF-CLSS.

Subjects were grouped based on language performance: Low language subjects (15 ASD/0 TD) had CELF-CLSS scores more than one standard deviation below the norm (CLSS < 85), those with typical language (15 ASD/7 TD) were within a single standard deviation of the norm (85 ≤ CLSS ≤ 115) and those with above normal language skill (5 ASD/8 TD) were above a standard deviation above the norm (CLSS > 115). Figure 3b shows group mean and standard errors of age/token/hemisphere-corrected ERD for these categories, illustrating the general increase of ERD integral with increasing language ability. Although independent post hoc analysis examining potential effects of ASD and language category within the combined typical and high language groups failed to reach statistical significance (ASD: 144.6 ± 17.5; TD: 116.4 ± 18.7, $p = 0.288$/typical language: 121.9 ± 16.1; high language: 139.0 ± 20.3; $p = 0.5$), in both groups the increased ERD attributed to ASD diagnosis was of similar magnitude to that found using the entire cohort. This suggests that the qualitative increase in ERD of ASD subjects (compared to TD) matched for language ability seen in Fig. 3a exists across language abilities and is not the result of an over correction for the CELF-CLSS dependence.

Post-hoc analysis investigating the left and right auditory cortices separately revealed a bilateral ERD-CELF-CLSS

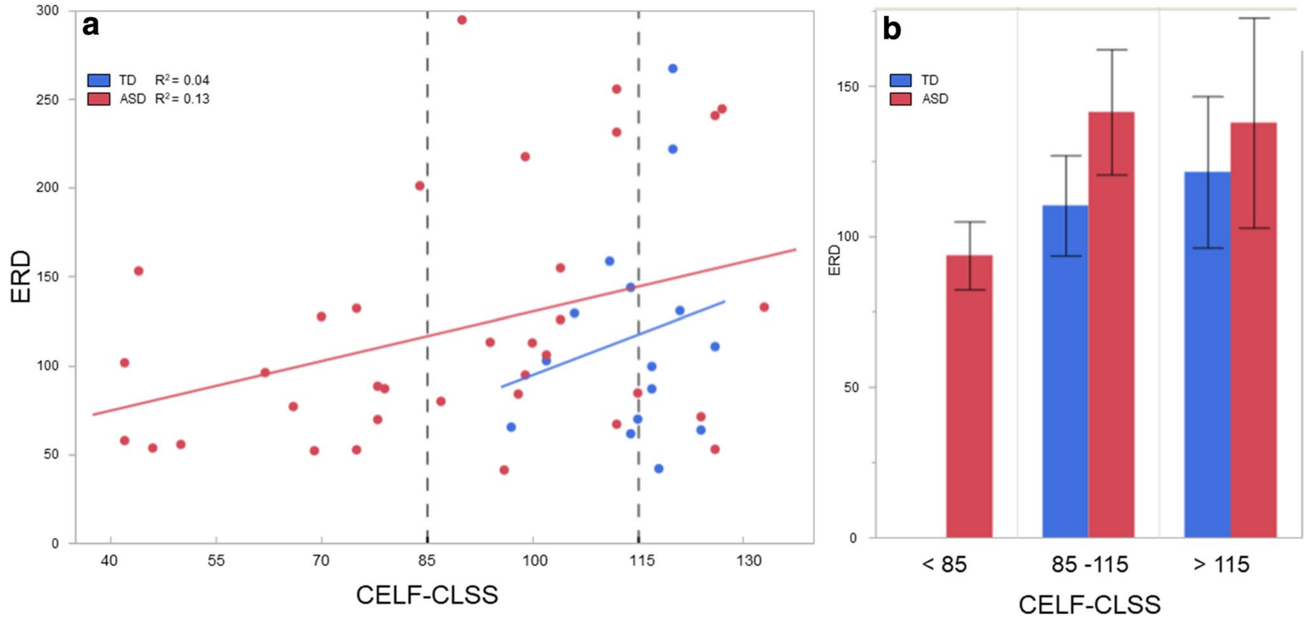

Fig. 3 **a** Scatter plots of age, token and hemisphere corrected ERD integral (ERD) versus CELF-CLSS, show similar relationships for both ASD (red) and TD (blue) subjects. **b** Grouping subjects based on CELF-CLSS illustrates a qualitative elevation in ERD integral in ASD subjects (compared to TD) matched for language ability

relationship (Left: slope = 0.80, F ratio = 3.6, p = 0.06, Right: slope 1.1, F ratio 4.7, $p = 0.035$). The qualitative ASD effect was not statistically resolved in the right auditory source, while a weak trend was observed in the left auditory source (ASD: 127.2 ± 11.6, TD: 90.1 ± 18.9, $p = 0.12$).

For regression analyses, examining the ASD cohort alone, neither PRI nor ADOS-CSS demonstrated significant relationships with ERD integral (both $ps > 0.05$). PRI did, however, account for a portion of the variance in ERD integral; when entered first PRI explained 9.1% ($p = 0.09$) and CELF-CLSS (entered second) accounted for an additional 4.0% ($p = 0.24$). However, when the order was reversed, CELF-CLSS accounted for a statistically significant 12.7% ($p < 0.05$) of the variance in ERD and PRI (entered second) did not account for significant additional variance ($R^2 = 0.1\%$, $p = 0.89$). In our cohort, we determined that PRI and CELF-CLSS were in fact highly correlated ($R^2 = 60\%$, $p < 0.001$); thus, it seems that the PRI partly explained ERD variance by virtue of it being a proxy for CELF-CLSS (since order of entry impacted findings). ADOS-CSS did not account for significant variance either when entered first or second, suggesting that the ERD integral is specifically an index of *language* ability across the cohort and not confounded by severity of autism symptoms per se.

Discussion

In this study we examined the oscillatory response of the superior temporal gyrus (STG) to basic lexical information using an interleaved word/non-word paradigm. While traditionally associated with auditory sensory processing, the STG also plays a central role in models of receptive language function, as it contains primary auditory and auditory association cortex (see Hickok and Poeppel (2000), Kandel et al. (2000) for a general discussion of language networks). The main finding of the study is the introduction of an MEG measure of language ability, the integral of 5–20 Hz event related desynchronization occurring 200–1000 ms post stimulus. While sufficient temporal resolution to quantify oscillatory activity (on the order of tens of milliseconds, precluding the use of slower techniques such as fMRI) is available using EEG, the improved source modeling capabilities of MEG motivates its use in this study. Our findings show that ERD in the 5–20 Hz, 200–1000 ms time–frequency range indexes language ability in both neurotypicals and children across the autism spectrum. This parameter does not show strong age dependence, but correlates with a clinical measure encompassing both expressive and receptive language in both the whole cohort and the ASD group alone. It appears that the integral of the ERD is increased in line with language ability, perhaps reflecting the quality and depth of lexical search and processing underlying increased language ability.

Prior MEG studies that have investigated the oscillatory response to word class stimuli have observed late field ERD in the alpha and beta bands in healthy adults (Brennan et al. 2014; Tavabi et al. 2011) and in parents of ASD children (McFadden et al. 2012). Similar to the findings of McFadden et al. (2012), we did not observe a significant effect of group on late field ERD. Unlike Tavabi et al. (2011), who observed increased ERD in response to words compared with non-words, in this study no main effect of stimulus token on ERD activity was observed. Increased ERD was observed by (Brennan et al. 2014) during semantic priming (i.e. more ERD observed with unrelated tokens compared to related tokens) and during the recognition phase (vs. encoding) of auditory EEG memory task in children using (Krause et al. 2007) supporting the notion that ERD may be modulated by memory access (lexical or otherwise).

It is noteworthy that non-words in fact exhibited strong relationships between ERD and language ability (in fact trending to be stronger than the relationship elicited by word tokens). This slightly counterintuitive observation may be reconciled by considering the pronounceable and plausible nature of the non-word tokens (e.g. "blick"), which perhaps elicit strong lexical activity (in an attempt to search for and establish the lexical item), as opposed to the non-word tokens used by Tavabi et al. (2011) which while word like in prosody were unintelligible. This interpretation is supported by the fact that pronounceable non-words induce robust effects related to lexical search, a finding that is well-established in the behavioral literature, where items of this type are found to induce delays in reaction times in lexical decision relative to existing words (Murray and Forster 2004). It is also consistent with the recognized notion of language impairment assessment via "non-word" repetition task ability (Bishop et al. 1999; Bishop et al. 1996; Gallon et al. 2007).

While increasing ERD is associated with increasing language ability, it is of note that there is a non-significant tendency for children with ASD to have *elevated* ERD integrals compared to their language-matched typically developing peers (as evidenced by the y-axis shift between ASD and TD regression lines in Fig. 3a, and the bar charts of Fig. 3b). As such, we conclude that the ERD relates to language impairment/ability per se with no modulation by ASD status. However, if the non-significant tendency for individuals with ASD to show elevated ERD compared to language-ability matched TD peers is borne out in larger sample studies, or under more probing linguistic challenges, it would be tempting to speculate that the observed ERD elevation in ASD could reflect an inefficiency in the coupling between auditory cortex oscillatory activity and subsequent determinants of language performance. Recognizing the hypothesis as initially counterintuitive, one hypothesis is that the observed ERD elevation could represent "additional" resources being allocated in ASD to achieve similar levels of language performance as their TD peers. Larger scale examinations of this hypothesis are thus warranted. Overall, examining ERD integral as a function of CELF-CLSS *across* the autism spectrum allows us to embrace the individual differences in ASD phenotype (at least in terms of language ability) rather than attempting to assess "group" contrast effects, given the known heterogeneity of the ASD population.

We support the contention that this late field oscillatory activity is specific to language ability by establishing the non-relation with general cognitive ability (indexed by the non-verbal IQ, perceptual reasoning index) or with general autism severity (the CSS of the ADOS), except to the degree that these measures are proxies for language ability itself. It remains to be elucidated if this measure has a similar relationship with language ability in other non-ASD populations.

Conclusion

In this study we focus on the oscillatory response of the auditory cortex to basic lexical information using an interleaved word and pronounceable non-word paradigm. In this paradigm it appears that ERD of the auditory cortex between 5 and 20 Hz, 200 and 1000 ms post stimulus tracks with the clinically-assessed language ability in children with ASD and their neurotypical peers. In both cohorts, increases in ERD predict increased language ability. As a measure derived from a passive paradigm, ERD does not depend on the participant complying with or completing task instructions, suggesting its applicability to studying populations that have difficulty doing so. The potential uses of such an objective index of language ability would include the investigation of lower functioning children with ASD (in whom diminished ERD would be predicted) as well as in younger children where ERD would be hypothesized to increase during language acquisition. Finally, as a biomarker of intact language processing (at least, lexical access), it would appear this measure might have utility during language therapeutic interventions (either behavioral or pharmacologic).

Acknowledgments We would like to the thank all of the participants and their families for their cooperation and for participating in this study. This work was supported in part by NIH R01DC008871 (TR), NIH R01HD073258 (DE), NIH K01MH108762 (LB) and NIH

U54HD086984, the institutional IDDRC (TR directs the Neuroimaging Neurocircuitry Core).

Authors Contribution LB, Ph.D. is a Research Scientist at the Lurie Family Foundations MEG Imaging Center at the Children's Hospital of Philadelphia (CHOP). KS, Ph.D. is a Post-Doctoral Researcher in the Radiology Department at CHOP and a Visiting Scholar in the Department of Linguistics at the University of Pennsylvania. LB, PhD, is a pediatric neuropsychologist in the Department of Child and Adolescent Psychiatry and Behavioral Sciences, the Center for Autism Research, and the Autism Integrated Care Program at CHOP. TPLR, PhD, is a professor of Radiology, Vicechair of Research for the Department of Radiology and the Oberkircher Family Endowed Chair in Pediatric Radiology at CHOP. DE, Ph.D. is a professor and chair of the Department of Linguistics at the University of Pennsylvania.

Compliance with Ethical Standards

Conflict of interest Dr. Roberts declares consulting agreements (medical advisory boards) with CTF MEG, Ricoh, Spago Nanomedicine, Avexis Inc. and Acadia Pharmaceuticals as well as intellectual property under licensing negotiation. Drs. Bloy, Shwayder, Blaskey and Embick declare no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Written informed consent was obtained from all participant's families and each participant (when competent to do so) gave verbal assent to participate in the study.

Glossary

ERD	Event related desynchrony—task related decreases in oscillatory power relative to baseline
ERS	Event related synchrony—task related increases in oscillatory power relative to baseline
MEG	Magnetoencephalography
EEG	Electroencephalography
ASD	Autism spectrum disorder
TD	Typically developing
M50/M100	Prominent middle and late components of the auditory evoked field
Lexical	Relating to the words or vocabulary
Theta Band	Oscillatory activity between 4 and 6 Hz
Alpha Band	Oscillatory activity between 8 and 12 Hz
Beta Band	Oscillatory activity between 13 and 30 Hz
Gamma Band	Oscillatory activity above 30 Hz (typically below 100 Hz)
STG	Superior temporal gyrus
ADOS-CSS	Calibrated severity score derived from the autism diagnostic observation schedule
PRI	Perceptual reasoning index from the wechsler intelligence scale for children-IV
CELF-CLSS	Core language standard score from the clinical evaluation of language fundamentals

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