Neural detection of changes in amplitude rise time in infancy

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ABSTRACT

Amplitude rise times play a crucial role in the perception of rhythm in speech, and reduced perceptual sensitivity to differences in rise time is related to developmental language difficulties. Amplitude rise times also play a mechanistic role in neural entrainment to the speech amplitude envelope. Using an ERP paradigm, here we examined for the first time whether infants at the ages of seven and eleven months exhibit an auditory mismatch response to changes in the rise times of simple repeating auditory stimuli. We found that infants exhibited a mismatch response (MMR) to all of the oddball rise times used for the study. The MMR was more positive at seven than eleven months of age. At eleven months, there was a shift to a mismatch negativity (MMN) that was more pronounced over left fronto-central electrodes. The MMR over right fronto-central electrodes was sensitive to the size of the difference in rise time. The results indicate that neural processing of changes in rise time is present at seven months, supporting the possibility that early speech processing is facilitated by neural sensitivity to these important acoustic cues.

1. Introduction

To acquire language, a child must be able to segment an incoming auditory stream into its separate phonetic, syllabic, lexical and other components, and to attach symbolic meaning to acoustic word forms. Infants utilise a range of acoustic cues to aid language learning. The neural literature shows that they are sensitive to rapidly-arriving pitch information (Hämäläinen et al., 2019), changes in duration (Richardson et al., 2003), F0 changes, and features like voice onset time (Guttorm et al., 2005, 2010; Leppänen et al., 2010; van Zuijen et al., 2013). The incoming stream of speech contains multiple such acoustic features that offer cues to its linguistic structure. In this study, we focus on "rise times" (rates of change) in the modulations in intensity (amplitude) that carry important linguistic information. Infant sensitivity to rise time has not previously been studied at the neural level.

Speech meets the human ear as a sound pressure wave whose shape ("amplitude envelope") contains temporal patterns that fluctuate over many different timescales. Rise times function as acoustic edges marking the onset of new phonological units. They are mechanistically important for speech comprehension (Ding and Simon, 2014; Doelling et al.,

2014). They trigger alignment between brain rhythms and speech rhythms, supporting neural encoding of the speech envelope (Giraud and Poeppel, 2012, for overview). The speech envelope is represented neurally throughout infancy (Kalashnikova et al., 2018; Jessen et al., 2019; Attaheri et al., 2022; Ortiz Barajas et al., 2021). Reduced perceptual sensitivity to amplitude rise times has been linked to both developmental dyslexia (difficulties in phonological processing) and Developmental Language Disorder (DLD, difficulties with syntax and grammar, e.g. Goswami et al., 2002; Pasquini et al., 2007; Richardson et al., 2004). Individual differences in infants' ability to detect changes in rise time could affect the fidelity with which linguistic information in the speech envelope is represented, helping to explain individual differences in later language outcomes. Behavioural evidence shows that perceptual sensitivity to differences in the rise times of non-speech sine tone stimuli is linked to receptive and productive vocabulary at three years of age (Kalashnikova et al., 2018, 2019). In the current study, we also used tone stimuli but recorded EEG, because neural data may reveal greater sensitivity to changes in rise time.

From one perspective, we might view speech as built of units like phonemes and syllables placed together to construct larger units of

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meaning like words and sentences. However, it may be more fruitful to view speech processing as perceiving a tree-like structure of amplitude modulations within the pressure wave, in which larger patterns provide hierarchically-organised form to smaller components (Liberman and Prince, 1977). This proposed linguistic hierarchy is reflected acoustically in the amplitude modulation (AM) structure of the speech envelope, in which the slowest modulations provide a nested structure for faster ones (Leong and Goswami, 2015). For young infants who cannot yet comprehend speech but nonetheless preferentially attend to it (Vouloumanos and Werker, 2004; Spence and DeCasper, 1987), speech rhythm may provide a predictive temporal framework upon which to build their language acquisition. Rise time is a key acoustic component of perceived rhythm (Greenberg, 2006), and rhythm has long been recognised as a precursor of language acquisition (Mehler et al., 1988; Nazzi et al., 1998). Accordingly, sensitivity to rise time may play a key role in infants' ability to utilise speech rhythm patterns during language learning.

Prior infant ERP studies of other language-relevant acoustic features document a number of changes over the first year of life. Auditory ERPs in infants become larger from birth for repeated sounds (Kushnerenko et al., 2002b; Lippé et al., 2009) and ERPs become either larger or smaller for change detection responses depending on the polarity of the ERP response (Choudhury and Benasich, 2011; Kushnerenko et al., 2002a; Ortiz-Mantilla et al., 2016). Early research on the auditory mismatch response (MMR), a measure of change detection, found a positive peak in the infant difference wave about 250 ms post-stimulus, rather than the anticipated mismatch negativity (MMN; Dehaene-Lambertz and Dehaene, 1994). A MMN is seen as a more mature response than the positive MMR (Friedrich et al., 2004), with its emergence linked to age and language exposure (Garcia-Sierra et al., 2011), stimulus type (Cheng et al., 2015), and the size of contrast between stimuli (Cheng and Lee, 2018). Accordingly, morphological changes to rise time MMRs would be expected over the first year of life.

We used an ERP-based mismatch paradigm during a longitudinal infant project ("BabyRhythm"), conducted when infants were seven and eleven months of age. Following the behavioural report by Kalashnikova, Goswami and Burnham (2018), we examined whether infants could discriminate a standard stimulus with a short rise time (15 ms) against stimuli with longer rise times. Our aim was to investigate whether the neural thresholds for detection of changes in rise time differ from those seen when an overt behavioural response is required. Behavioural measures provide information about an infant's perception of a stimulus, but it is possible that before the infant can make a behavioural response, developmental changes in auditory processing may be occurring at a neural level. Infants track the amplitude envelope from birth (Kalashnikova et al., 2018; Jessen et al., 2019; Attaheri et al., 2022; Ortiz Barajas et al., 2021) and thus, given that rise time discrimination plays a role in adult speech tracking, we would expect that neural mechanisms of rise time detection should be present in the infant brain. Plakas et al. (2013) used an ERP approach to study rise time detection in young children, and found a MMN to a single amplitude rise time sine tone oddball among typically-developing children at 41 months of age. In the present study, we also measure MMNs, but instead of presenting a rise time oddball of a fixed length, we vary the rise time oddball on an interval scale. By manipulating the length of the rise time oddball, we can examine, on both an individual and a group level, the limits of infants' rise time discrimination capability. Our primary hypothesis was that infants would exhibit a mismatch response to amplitude rise time oddballs. We anticipated that this response would become smaller as the difference in rise time between the standard and the oddball (henceforth, rise time difference) became smaller.

We examined three additional factors which make a novel contribution to the infant rise time literature. First, we hypothesised that the mismatch response would be less positive for older infants, reflecting the transition from MMR to MMN. Interactions between rise time difference and age could be expected at the neural level, as there is behavioural

change in rise time sensitivity between seven and ten months for infants not at risk for dyslexia (Kalashnikova et al., 2018, 2019). Second, we were interested in whether infants' detection of changes in rise time would be facilitated by a stimulus more acoustically similar to speech, speech-shaped noise (SSN). SSN is used in Dutch studies of rise time discrimination by children (e.g. Law et al., 2017) because it has similar temporal features to speech. Accordingly, we varied whether the stimuli were presented as sine tones or SSN. We anticipated that rise times of the SSN stimuli, given their temporal speech-like features, may be more easily discriminated by infants. Differences in neural detection of stimuli with speech-like features, relative to tone stimuli, may also be informative in relation to the role of rise time detection in speech tracking and possible variations with age.

Finally, we compared responses across the fronto-central electrodes. These electrode groups were identified for their role in rise time mismatch detection in older children by Plakas et al. (2013) and Peter et al. (2016). Sensitivity to temporal acoustic features can differ by hemisphere. More rapid temporal transitions, related to phonemic information, appear to be preferentially processed in the left hemisphere (Boemio et al., 2005). Slower auditory modulations, those associated with prosodic and syllabic processing, may be preferentially processed in the right hemisphere, which is also associated with rhythm perception (Sammler et al., 2015). In the current study, we take a scalp-level approach due to the difficulty in attaining accurate source-localised results in infants, especially across different ages (Lew et al., 2013; Noreika et al., 2020). Nonetheless, topographical results may show differences between electrode groups by picking up different levels of activity from different sources or due to developmental change. Topographical results may also inform comparisons with related research with older children. Temporal sampling theory has hypothesised that atypical processing of slower modulations in speech may be right-lateralised, and this has been found to be the case in neural speech tracking studies with older children with dyslexia (Di Liberto et al., 2018).

2. Methods

2.1. Participants

Participants were infants enroled in a longitudinal, multi-measure study of early auditory processing and language acquisition. Infants were recruited as a community sample and their parents provided informed consent. At the age of seven months, 113 infants were enroled in the study, and 109 infants took part in the rise time study. At the age of eleven months, 100 infants received the rise time stimuli. Missing sessions are accounted for in the supplementary materials. During preprocessing and data cleaning, technical issues were diagnosed and resulted in the exclusion of two seven-month-old and four eleven-month-old EEG sessions due to missing triggers in the EEG data, and one seven-month-old session due to no sound being played in the EEG booth during recording. The data included in the current analyses are from 74 infants at seven months and 96 infants at eleven months, among whom 64 infants contributed data at both ages. The average ages at the time of recording were 7 months, 3 days (SD = 5 days) and 11 months, 2 days (SD = 5 days). The study was approved by the Psychology Research Ethics Committee of the University of Cambridge, U.K. REDCap (Research Electronic Data Capture; Harris et al., 2009, 2019) database software was used to store and manage information about the data.

2.2. Stimuli

The standard stimulus with which infants were presented had a rise time of 15 ms. The ten oddball stimuli had longer rise times ranging from 161.1 ms to 292.7 ms, in steps of 14.6 ms. In each lab session, infants were played all auditory stimuli – standards and oddballs – exclusively in the form of either a sine tone or SSN. Of the infants included in the

analysis, 37/74 received SSN and 37/74 received sine tone stimuli at seven months. At eleven months 50 heard the SSN and 46 heard the sine tone stimuli. Of the 64 included infants who attended both sessions, 15 heard the sine tone both times, 24 heard the SSN both times, and 25 heard a different stimulus type each time.

2.3. Procedure

EEG data were recorded at a rate of 1000 Hz via a 64-channel EGI Geodesic Sensor Net and GES 300 amplifier (Electrical Geodesics Inc., Eugene, OR, USA) with four facial electrodes removed. Infants were seated in a soundproof acoustic chamber, in a high-chair or occasionally on a parent's lap. They were seated approximately 65 cm away from a presentation screen. Auditory stimuli were played through speakers placed either side of this screen (Q Acoustics 2020i), via an amplifier (Cambridge Audio Topaz AM5 Stereo).

The auditory stimuli were played in blocks. There were five blocks with 48 auditory stimuli each, of which 16.67% were oddballs. The first oddball presented was the deviant with the longest rise time, that is, the one with the largest difference from the standard stimulus' rise time. There were four to nine standard stimuli between the oddballs, and every fifth oddball decreased in rise time from the previous one.

To keep infants occupied during the 5-minute EEG recording, a silent black-and-white cartoon played on the presentation screen. This EEG-based rise time detection paradigm was presented at the start of a longer data collection session including auditory and audiovisual EEG, eye-tracking and motion-capture paradigms. Videos and auditory stimuli were presented using scripts written in Matlab with Psychtoolbox (Brainard, 1997; Kleiner et al., 2007).

2.4. EEG preprocessing

Data were filtered via EEGlab (Delorme and Makeig, 2004), with a highpass filter of 0.2 Hz and a lowpass filter of 45 Hz. The data file for each participant was inspected to identify persistently bad channels (e.g. broken electrodes, poorly fitting electrodes exhibiting extreme fluctuations in amplitude). Of the 60 channels on the infant cap, two were always identified for rejection (channels 23, 55) as they rarely fit flush to the infant's skin. On average, 3.9 additional persistently bad channels were identified per recording, with a standard deviation of 3.01 channels. During infant EEG testing sessions, channels may become noisy – transiently or persistently - due to the infant touching their head, shifting position, or engaging in gross movement. Data cleaning was therefore performed on epoched data in a number of steps – first, identifying bad channels epoch by epoch, and rejecting and interpolating these transiently bad channels alongside the persistently bad channels; second, running both automated and manual procedures for identifying epochs with artefacts remaining after bad channel interpolation; and third, rejecting epochs based on agreement between the automated and manual bad epoch identification procedures. Epochs ran from 160 ms before the onset of the stimulus to 800 ms after, with the 160 ms before stimulus onset used as baseline. Further details on these steps, including the use of ERPlab software (Lopez-Calderon and Luck, 2014) are given in the Supplementary materials.

When the cleaned and epoched data were split into standard and oddball epochs, there were on average 169.05 (SD = 30.21) epochs in response to standard stimuli and 31.78 (7.15) to oddball stimuli. Table 1 gives the mean number of epochs per stimulus in each age group as well as the range (further explanation of "matched standards" is given in the section below). After the rejection of epochs with artefacts, the data were re-referenced to the whole head, with the exclusion of 9 peripheral channels near the neck, ears and forehead.

2.5. Data analysis

The average ERP in response to each stimulus was calculated over

three subgroups of electrodes corresponding to FC3, FCz and FC4 and their neighbours.[1] Due to the greater number of standard than oddball stimuli, the standard stimulus ERP was derived from the epoch preceding an oddball stimulus. These epochs were determined in advance of data cleaning, to ensure that both rise time oddball and standard epochs had a similar probability of being missing. The average ERP in response to these standard stimuli was subtracted from the average ERP in response to the corresponding oddball stimulus. The window of interest for the analyses was 300–460 ms post-stimulus. This is a typical mismatch response window for infants (e.g. Dehaene-Lambertz and Dehaene, 1994; Friedrich et al., 2004) while also allowing for the longest stimulus rise time (293 ms) to have concluded. Cluster-based permutation testing was applied post-hoc to confirm the appropriateness of these electrode groups and of the time window for analysis (see Supplementary information).

Difference waves with a mean amplitude in the window of interest exceeding the mean (across all infants, regions of interest, and oddball rise time lengths) $\pm$ 3 times the standard deviation were excluded as outliers. This equated to 1.34% of all data points. A set of comparison difference waves (henceforth, the "matched standards") were computed by subtracting each of the standard ERPs used to calculate the mismatch peak from another standard ERP. This was done to ensure that results reflected differences in processing of standard and oddball stimuli, and not the fact that ERPs in response to any stimuli may differ from one another by chance, especially when computed from a limited number of trials as in this study. A similar approach, referred to as "dummy standards", was used in research by Bishop and Hardiman (2010), who also wanted to ensure that results were not driven by false positives.

Following outlier exclusion, the difference wave data from the mismatch window and the baseline window was entered in linear regression models to find whether there was, overall, a significant mismatch peak; whether it differed from the matched standard peak; if it was affected by stimulus type (sine tone or SSN); how it changed with age; how it differed by electrode location; and how it varied depending on how similar or different the oddball stimulus was to the standard.

We compared difference wave amplitude in the baseline window to that in the window of interest as another means of examining whether there was a mismatch peak in the data. Amplitude in the baseline window approximates zero, and thus a significant difference between difference wave amplitudes in the baseline window and those in the window of interest suggest the presence of a mismatch peak in the data; if the difference wave in the window of interest also approximates zero, this suggests that no peak is present. The use of the baseline window to ascertain the presence of a peak is also used in Foxe and Simpson (2002).

Statistical analyses were run using the lme4 and lmerTest packages in R (Bates et al., 2007). Regression analyses allow for the inclusion of both categorical independent variables (such as age) and continuous ones (such as the difference in rise time between the standard and the oddball). Furthermore, the application of a Linear Mixed-effects Model (LMM) allows for the inclusion of the data that we do have for a given infant even if they missed an appointment or had data from one electrode subgroup excluded due to outlier values. For the same reason, a mixed effects approach has been previously used in infant ERP research (Stahl et al., 2010), including in auditory paradigms (Begum-Ali et al., 2021) and specifically a mismatch paradigm (Zhao and Kuhl, 2021).

Please note also that rise time difference is treated as continuous by the LMM. This is because differences in rise time length are differences of scale, not category. Designating rise time as a continuous variable ameliorates the potential issue of some oddball intervals having at least one infant who did not contribute any valid epochs (Table 1), as the linear trend across rise time differences can still be computed. Including more epochs in each calculated ERP (e.g. by collapsing rise time difference into two categories of "long" and "short") might reduce the noise

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[1] FC3: EGI electrode numbers 14, 15, 19; FCz: 4, 7, 54; FC4: 53, 56, 57.

Table 1

Mean and standard deviation of epochs per rise time stimulus per age, by stimulus type, after removal of noisy epochs.

Oddball rise time length in ms	293	278	263	248	234	220	205	190	176	161
7 months mean oddball epochs per sine ERP (SD, min-max)	3.22 (1.25, 0–4)	3.3 (1.1, 0–4)	3.35 (0.79, 1–4)	3.08 (0.98, 0–4)	3.08 (1.04, 1–4)	3 (1.13, 0–4)	3.3 (0.88, 1–4)	3.08 (0.95, 1–4)	2.86 (1.27, 0–4)	3.03 (0.99, 0–4)
7 months mean standard epochs per sine ERP (SD, min-max)	3.05 (1.27, 0–4)	3.19 (1.1, 0–4)	3.35 (0.95, 0–4)	3.27 (0.8, 2–4)	3.11 (0.84, 1–4)	3.05 (1.03, 1–4)	3.27 (0.87, 1–4)	2.97 (1.07, 0–4)	2.86 (1.16, 0–4)	2.97 (1.07, 0–4)
11 months mean oddball epochs per sine ERP (SD, min-max)	3.28 (0.83, 1–4)	3.2 (0.98, 0–4)	3.35 (0.92, 1–4)	3.43 (0.83, 1–4)	3.35 (1.02, 0–4)	3.15 (1.25, 0–4)	3.24 (0.9, 1–4)	3.48 (0.78, 1–4)	3.28 (1.09, 0–4)	2.87 (1.24, 0–4)
11 months mean standard epochs per sine ERP (SD, min-max)	3.3 (0.96, 0–4)	3.3 (0.92, 0–4)	3.41 (0.88, 1–4)	3.2 (0.86, 1–4)	3.3 (0.99, 0–4)	3.33 (1.03, 0–4)	3.17 (0.93, 1–4)	3.09 (1.21, 0–4)	3.29 (0.83, 1–4)	3.09 (1.35, 0–4)
7 months mean oddball epochs per SSN ERP (SD, min-max)	3.51 (0.87, 0–4)	3.43 (0.87, 0–4)	3.41 (0.9, 1–4)	3.49 (0.73, 2–4)	3.3 (0.85, 1–4)	3.3 (0.97, 0–4)	3.19 (0.97, 0–4)	3.11 (1.05, 0–4)	3 (1.08, 0–4)	2.86 (1, 0–4)
7 months mean standard epochs per SSN ERP (SD, min-max)	3.35 (0.95, 0–4)	3.43 (0.9, 1–4)	3.27 (1.07, 1–4)	3.43 (0.73, 2–4)	3.41 (0.8, 1–4)	3.16 (1.04, 0–4)	3.19 (1.04, 0–4)	3.03 (1.09, 0–4)	3.03 (1.07, 0–4)	3 (1.13, 0–4)
11 months mean oddball epochs per SSN ERP (SD, min-max)	3.14 (1.01, 0–4)	3.26 (1.03, 0–4)	3.08 (1.12, 0–4)	3.16 (0.98, 0–4)	3.24 (1.04, 0–4)	3.12 (1.12, 0–4)	2.9 (1.28, 0–4)	3.04 (1.28, 0–4)	3.08 (1.32, 0–4)	2.72 (1.21, 0–4)
11 months mean standard epochs per SSN ERP (SD, min-max)	3.1 (0.99, 0–4)	3.22 (1.07, 0–4)	3.22 (0.91, 1–4)	3.08 (1.03, 0–4)	3.24 (1.1, 0–4)	3.16 (1.23, 0–4)	3.1 (1.13, 0–4)	2.98 (1.15, 0–4)	2.82 (1.4, 0–4)	2.88 (1.3, 0–4)

in each difference wave, but would also mean that each difference wave would be computed from non-identical stimuli. Providing more data-points along the rise time difference continuum per participant to the LMM and including a random intercept on participant identity means that the model can work around the noise we might otherwise aim to remove by averaging over more epochs.

Finally, we explored whether each infant, at each age, had exhibited a mismatch response to each of the oddball stimuli. This was done by finding, for each individual infant, the 95% confidence interval of the amplitude of the difference waves, across all oddball stimuli, in the
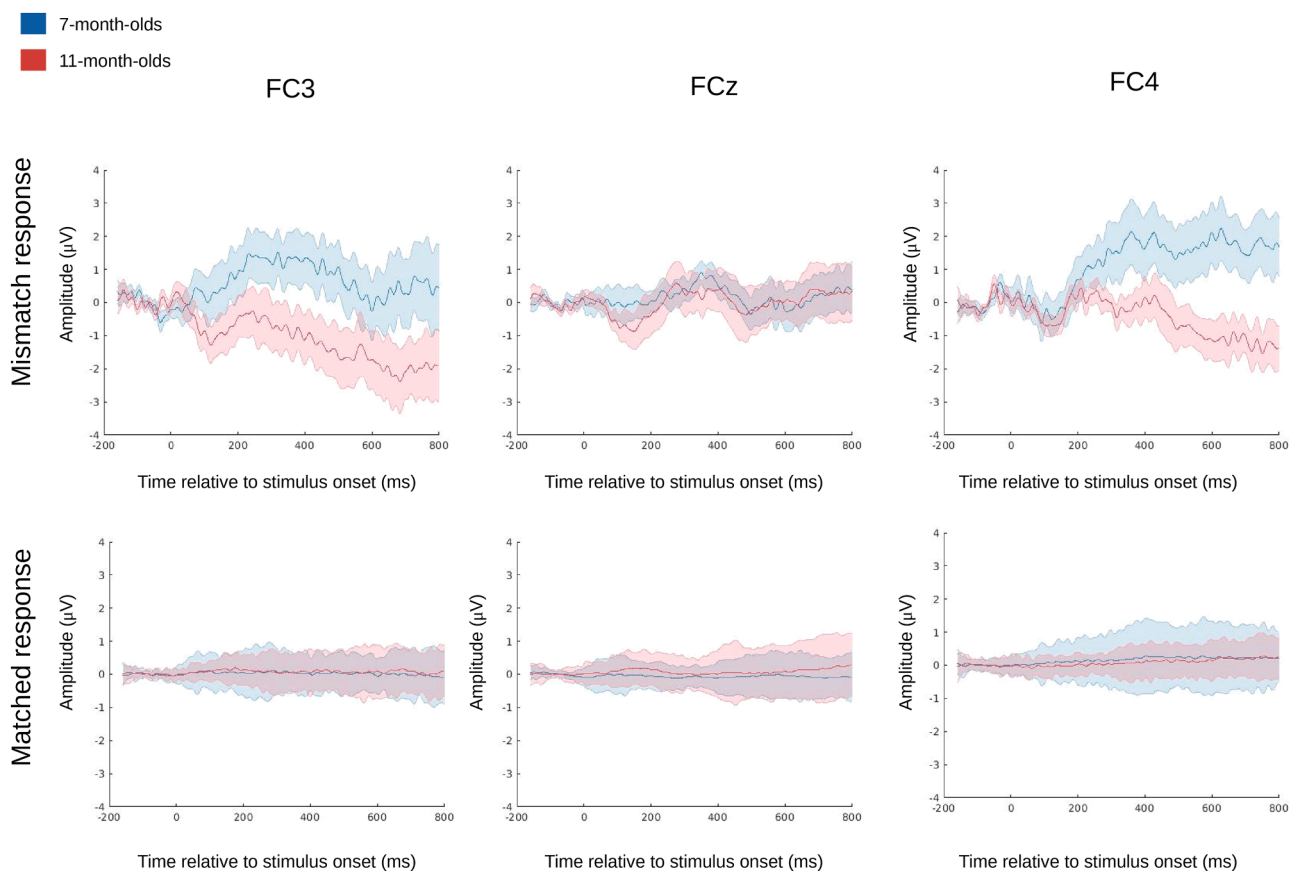

Fig. 1. Average difference waves at seven (blue) and eleven (red) months of age, over electrode groups. Top row shows the mismatch response between ERPs to standard and oddball stimuli, bottom row shows the "matched standard" difference waves between ERPs in response to different standard stimuli. Shaded regions denote the standard error of the mean response.

baseline period. If the mean amplitude of the window of interest in a particular oddball's difference wave exceeded the upper or lower bounds of this interval, this was characterised as a mismatch response. We could then determine at which point in the experiment, in response to which oddball stimulus, the infants stopped exhibiting a mismatch response. We expected this to allow us to infer each individual's detection threshold, providing an individual differences measure to regress against neural entrainment and language acquisition data from other timepoints in the BabyRhythm project.

3. Results

3.1. Difference wave results

The mean amplitude of the difference wave in the window of interest (300–460 ms post-stimulus) was 0.414 μV (SD = 3.467) averaged across all oddballs. At seven months, this value was 1.06 μV (SD = 3.114) and at eleven months it was − 0.084 μV (SD = 3.655). An initial model (Eq. (1)) was run to determine whether there was, overall, a peak in the window of interest that differed from the baseline window:

Difference Wave$_i$ = β_{0i} + β_1Window$_i$ + β_2Age$_i$ + β_3Window * Age$_i$ + u$_{0i}$ + ε_i, where i = participant identity. (1)

The presence of such a peak would indicate a mismatch response. An interaction with age would indicate whether the mismatch response differs by age, for example whether a more negative MMN response was present at eleven months but a positive MMR at seven months. The difference waves are shown in Fig. 1. ERPs to standard and oddball stimuli can be seen in Fig. A1 in the Supplementary material, illustrating that standard and oddball responses both follow a typical infant auditory ERP morphology. F tests using a Satterthwaite approximation method reveal a significant contribution to the model of age, F(1, 3757.9) = 9.375, p = 0.002, and of the interaction between age and window, F(1, 9547.9) = 9.435, p = 0.002, with a marginal contribution of window, F (1, 9549.1) = 3.083, p = 0.079. Model estimates reveal a significant effect of window, such that the amplitude of the response was larger in the window of interest than in the baseline window, β = 1.05, SE = 0.325, t = 3.23, p = 0.001. There was an interaction between age and window, such that the difference between difference waves in the window of interest and baseline window was smaller at eleven months, β = − 1.337, SE = 0.435, t = − 3.0729, p = 0.002. There was no main effect of age, β = − 0.007, SE = 0.308, t = − 0.022, p = 0.982, nor was the intercept significant, β = 0.011, SE = 0.235, t = 0.045, p = 0.964. The model fit was significantly better than that of the random model, χ^2 = 20.516, p = 0.0001. Including electrode group as a main effect and interaction term in this model does not affect the results (see Further Results in Supplementary materials).

T-tests were conducted separately for seven- and eleven-month-olds, taking the difference wave averaged across all oddballs. At seven months, there was a clear overall difference between the window and the baseline amplitudes, t(73) = 2.927, p = 0.005, CI = [0.338, 1.781], BF$_{10}$ = 6.41 (moderate to strong evidence for H$_1$). At eleven months, this effect was not present, t(95) = − 0.2243, p = 0.823, CI = [− 0.824, 0.657], BF$_{10}$ = 0.116 (moderate evidence for H$_0$). This suggests that, at seven months infants generally exhibited a positive MMR but at eleven months there was no consistent MMR or MMN.

In the matched data in which the standard responses in different blocks of the experiment were subtracted from one another, the mean amplitude in the window of interest was − 0.018 μV (SD = 2.03). This was − 0.014 μV (SD = 1.25) at 7 months and − 0.0223 μV (SD = 2.475) at 11 months. The mismatch response was then compared to this "matched" response. The aim of this approach is to investigate whether the peak previously observed in this window is specific to the mismatch response generated by comparing the size of the difference wave to the baseline, rather than an incidental peak that could occur when

subtracting any two ERPs from one another. The model was specified as in Eq. (2), with "Response Type" referring to whether the data was the mismatch response or the matched response. An effect of response type would suggest a difference in the neural mismatch response when a new stimulus was played, while an interaction with age would tell us whether the mismatch response changed with age (e.g. a larger MMR, or a shift to a MMN).

Difference Wave$_i$ = β_{0i} + β_1Age$_i$ + β_2Response Type$_i$ + β_3Age * Response Type$_i$ + u$_{0i}$ + ε_i, where i = participant identity. (2)

Model estimates reveal a significant effect of response type, such that the amplitude of the mismatch response was larger than the matched response in the window of interest (p = 0.019). There was a marginal interaction suggesting that the mismatch response was smaller at eleven months (p = 0.054). Full results are given in Table A1 and under Further Results in the Supplementary materials, including when electrode group is included in the model (which does not change the results). Taken together, the results show that there was a peak in the difference wave in the window of interest for the mismatch response, it was specific to the occurrence of an oddball stimulus, and it was more positive relative to the baseline at seven than eleven months.

3.2. Stimulus type

Stimulus type (sine tone or speech-shaped noise) was added to the model in Eq. (1) to investigate whether detection of a change in rise time would be facilitated by a more speech-like auditory stimulus relative to a tone. This model again showed a significant contribution to the model of age (F(1, 3002.8) = 9.398, p = 0.002), and the window by age interaction (F(1, 9545.1) = 9.4024, p = 0.002), with a marginal contribution of window (F(1, 9546) = 3.0631, p = 0.08). None of the effects related to stimulus type made a significant contribution. The model fit was significantly better than that of the random model, χ^2 = 21.537, p = 0.003. There are simple effects of window (p = 0.005) and window by age (p = 0.01) but no significant effects or interactions involving stimulus type, see Table A2 in Supplementary materials for full model results. This suggests that the mismatch response was not affected by which stimulus type the infant heard. Inclusion of electrode group in the model does not affect these results.

Given that some infants heard the sine tone at seven months, and SSN at eleven months (or vice versa), a random slope was included on stimulus type. This model was flagged for having boundary issues (i.e. being overly complex for the underlying data). Nonetheless, the Satterthwaite F tests showed the same pattern of results (window, p = 0.08; age, p = 0.002, window by age, p = 0.002). Effects are reported in Table A2. In Table A3, effects of the Eq. (2) (response type) model are reported when stimulus type is included. Satterthwaite-corrected F-tests show no effect or interaction with stimulus type, only an effect of age (F (1, 9468) = 5.9449, p = 0.015) and a marginal age by response type interaction (F(1, 9468) = 3.6834, p = 0.055). Hence the conclusion that, as a group, infants in this study were equally responsive to sine tone rise times and SSN rise times is supported.

3.3. Rise time difference and electrode group

Regarding the effect of age on the difference wave, older infants may be more likely to show a nascent MMN and may be more sensitive to rise time differences that are less perceptually salient. Another model was run to establish whether the difference in the rise time between an oddball and the standard stimulus affected the overall difference wave in the window of interest. Rise time difference was entered into the model as the difference in milliseconds between the rise times of the oddball and standard stimuli. It was anticipated that the mismatch response would be larger when the rise time of the oddball was longer, making it easier to discriminate against the standard. An interaction

with age might mean that easier stimuli elicited a large positive response at seven months and a large negative response at eleven months. To examine potential topographical differences in the neural response, electrode group was also included in this model, which is specified in Eq. (3). Given the negative results for stimulus type reported above, stimulus type was not included in the model. The ERPs in response to the standard and oddball stimuli by electrode group are shown in Fig. 1.

Difference Wave$_i$ = β_{0i} + β_1Rise Time difference$_i$ + β_2Age$_i$ + β_3Location$_i$ + β_4Rise Time difference * Age$_i$ + β_5Rise time difference * Location$_i$ + β_6Age * Location$_i$ + β_7Rise Time difference * Location * Age$_i$ + u_{0i} + ε_i, where i = participant identity. (3)

There were significant contributions to the model of the age by location interaction, $F(2, 4653.4) = 6.445$, $p = 0.002$, and the age by location by rise time difference interaction, $F(1, 4653) = 6.245$, $p = 0.002$. The model fit was significantly better than that of the random model, $\chi^2 = 26.752$, $p = 0.005$.

The model estimates, given fully in Table 2, show the results when FC3 is used as the base case for the comparison across electrodes. There is an effect of age ($p = 0.024$), showing that the MMR becomes more negative as infants get older. Overall, the MMR over FC4 is more negative than that over FC3 ($p = 0.002$), but becomes more positive as infants get older ($p = 0.0004$). Relative to FC3, the effect of the size of the difference in rise time between the oddball and standard over FC4 is positive ($p = 0.002$), suggesting a larger or more positive response for larger differences in rise time. The three-way-interaction between age, rise time difference, and electrode location suggests that this difference in the size of the MMR by rise time length over FC4 attenuates with age, as depicted in Fig. A2 in the Supplementary materials.

The results of an additional model including the matched data and with the inclusion of response type as a variable largely accord with these results, albeit with the model having complexity issues. Satterthwaite-corrected F-tests show marginal effects of age by electrode group ($F(2, 9452) = 2.658$, $p = 0.07$) and age by electrode group by rise time difference ($F(2, 9452) = 2.79$, $p = 0.06$). Mirroring the original analysis, these effects are significant in interactions with response type (age by electrode group by response type, $F(2, 9452) = 4.012$, $p = 0.018$; age by electrode group by rise time difference by response type, $F(2, 9452) = 3.65$, $p = 0.026$). Effects and interactions reported in

Table 2 suggest that the negative-going response over FC4 is driven by the mismatch responses rather than the matched responses. The more positive response over FC4 as rise time increases also interacts with mismatch response type. This suggests that the positive effect on response amplitude over FC4 at 11 months is due to the mismatch response type and not the matched response type. Finally, the negative three-way interaction shown in Table 2 remains negative when it becomes a four-way interaction including response type.

A striking aspect of Fig. A2 is the similarity of the distributions of the difference waves across all the different rise time differences. Accordingly, Fig. 2 illustrates the values of the difference wave by age and location, showing the large dispersal of difference wave amplitudes and valences across participants.

3.4. Individual thresholds

In this experiment, a range of ten oddball stimuli were used. Some had rise times that were very different to the standard and others were more similar. Our intention was to find at which point each individual infant ceased to display a difference wave greater than the baseline confidence interval. This point would indicate their threshold, at which they no longer perceived the oddball as different from the standard stimulus. However, the proportion of infants exhibiting a differential response to each stimulus was broadly similar across all of the oddball stimuli, as shown in Fig. 3. This proportion was also similar across the two age groups, with 85.1% of responses at seven months showing a difference wave that exceeded the confidence interval, and 83.1% of responses at eleven months showing the same. However, the approximately 15% of responses without an apparent mismatch response were not generated by the same 15% of infants. This indicates that the anticipated pattern of responses "dropping off" after a certain point for each infant did not manifest. There was no consistent pattern to the presence or absence of mismatch responses.

A consistent within-participant pattern of MMRs and MMNs did not emerge either, as infants' responses exhibited a mix of valences across the range of stimuli – 45.76% of responses at seven months were positive, and 39.33% were negative. At eleven months, these figures were 39.96% and 42.96% respectively. Individual infants' thresholds could thus not be ascertained. It appears that by using prior behavioural data

Table 2
Results of model examining effects of rise time difference and electrode location, FC3 base case.

|	Eq. (3)				Eq. (3) incl. response type			
	Estimate	Standard error	t	p	Est.	Standard error	t	p
Mismatch response type (ref. matched)					3.22	4.13	0.78	0.435
Rise time difference	-0.015	0.014	-1.128	0.26	-0.006	0.014	-0.453	0.651
Mismatch * rise time difference					-0.009	0.019	-0.483	0.629
Age 11 months (ref. 7 months)	**-8.91**	**3.949**	**-2.256**	**0.024**	-1.51	3.926	-0.385	0.701
Mismatch * Age 11mo					-7.393	5.52	-1.339	0.181
FCz (ref. FC3)	-3.991	4.182	-0.954	0.34	-1.307	4.148	-0.315	0.753
Mismatch * FCz					-2.677	5.84	-0.458	0.647
FC4 (ref. FC3)	**-13.254**	**4.173**	**-3.176**	**0.002**	2.051	4.149	0.494	0.621
Mismatch * FC4					**-15.29**	**5.834**	**-2.621**	**0.009**
Rise time difference * Age 11mo	*0.032*	*0.018*	*1.743*	*0.081*	0.006	0.018	0.355	0.722
Mismatch * Rise time difference * Age 11mo					0.025	0.025	0.998	0.319
Rise time difference * FCz	0.015	0.019	0.801	0.423	0.004	0.019	0.188	0.851
Mismatch * Rise time difference * FCz					0.012	0.027	0.44	0.66
Rise time difference * FC4	**0.061**	**0.019**	**3.169**	**0.002**	-0.009	0.019	-0.467	0.64
Mismatch * Rise time difference * FC4					**0.07**	**0.027**	**2.6**	**0.009**
Age 11mo * FCz	6.743	5.594	1.205	0.228	-0.262	5.543	-0.047	0.962
Mismatch * Age 11mo * FCz					6.999	7.808	0.896	0.37
Age 11mo * FC4	**19.755**	**5.592**	**3.532**	**0.0004**	-1.943	5.547	-0.35	0.726
Mismatch * Age 11mo * FC4					**21.68**	**7.81**	**2.775**	**0.006**
Rise time difference * Age 11mo * FCz	-0.025	0.026	-0.962	0.336	0.004	0.026	0.146	0.884
Mismatch * Rise time difference * Age 11mo * FCz					-0.003	0.036	-0.794	0.427
Rise time difference * Age 11mo * FC4	**-0.088**	**0.026**	**-3.428**	**0.0006**	0.006	0.026	0.251	0.802
Mismatch * Rise time difference * Age 11mo * FC4					**-0.095**	**0.036**	**-2.634**	**0.008**
Intercept	4.655	2.946	1.58	0.114	1.409	2.95	0.479	0.632
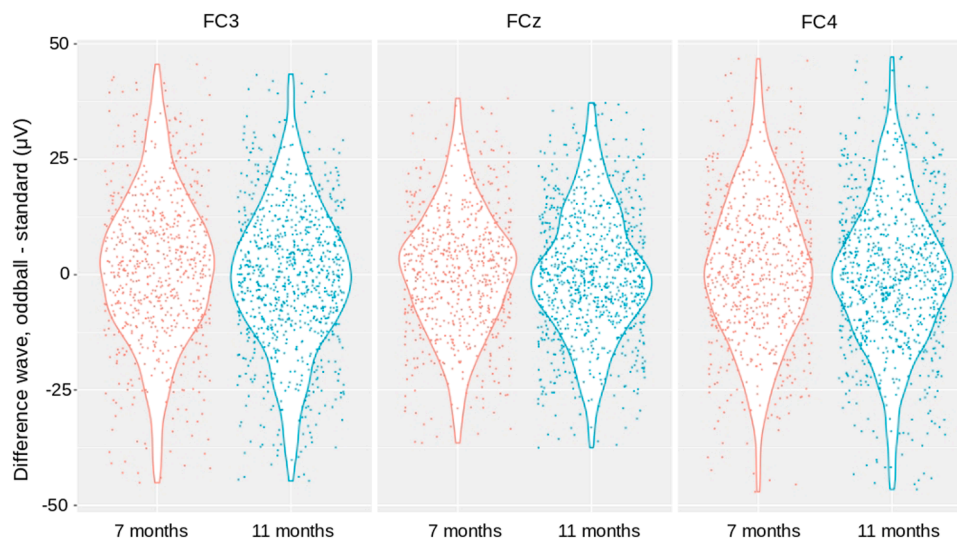
Fig. 2. Distribution of difference waves at seven and eleven months, across three electrode groups. Each dot represents a difference wave for a particular infant; there are up to ten dots per infant (one difference wave for each oddball rise time presented).
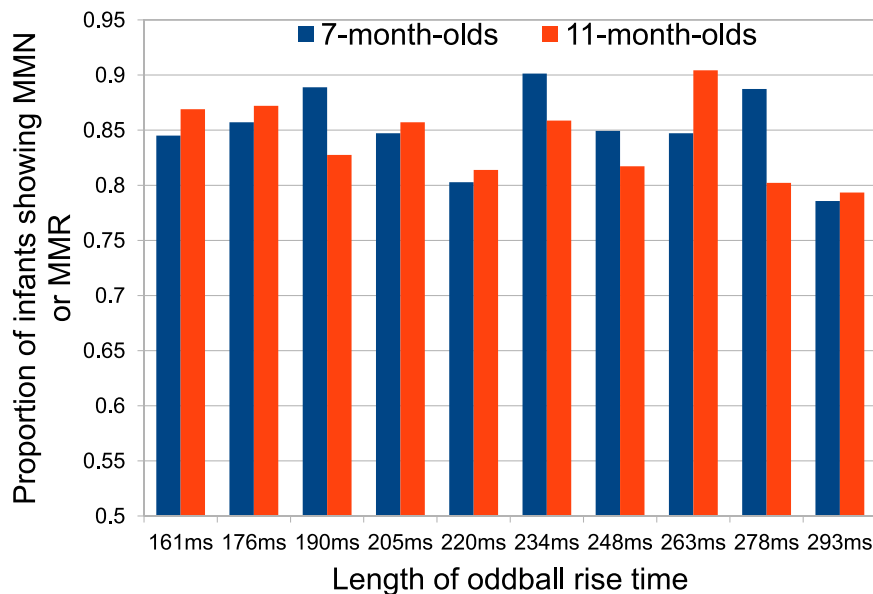

Fig. 3. Proportion of infants exhibiting, in response to each oddball stimulus, a difference wave in the time window of interest that exceeded (positively or negatively) the confidence interval of the baseline difference wave across all stimuli. Proportions are averaged across electrode groups. From left to right, the length of oddball rise time goes from the most similar to the standard stimulus, to the least similar.

to guide our stimulus selection, we underestimated infant sensitivity to rise time.

4. Discussion

Here we show that the infant brain exhibits a neural response to changes in amplitude rise times, as predicted. Further, the neural response was similar whether the stimulus was a sine tone or SSN. Contrary to expectation, the infant brain showed a robust mismatch response to the full range of ten rise times utilised here. The consistent neural detection of changes in rise time, even for oddballs expected (from behavioural data) to be below perceptual threshold, indicates that rise time cues are available to infants from as young as seven months of age. This constitutes the first neural evidence for robust detection of changes in rise time in infants, and extends prior behavioural data (Kalashnikova et al., 2018). A neurophysiological approach thus

suggests that perception of the different rise times that contribute to extraction of the AM hierarchy in IDS (Leong et al., 2017) is well-developed by seven months in typically-developing infants.

A negative shift in the mismatch response was observed with age. The difference wave in the window of interest relative to the baseline window was larger at seven than at eleven months of age (see Eq. (1) model). Further, the difference in the mismatch difference wave was greater than the "matched standards" difference wave at seven but not eleven months (see Eq. (2) model). We interpret these age effects as indicating a shift towards the MMN, in line with other developmental literature showing this transition from MMR to MMN (Friedrich et al., 2004; Garcia-Sierra et al., 2011). While the ability to discriminate some auditory stimuli is lost during infancy due to perceptual narrowing, rise time discrimination remains present in childhood (e.g. Goswami et al., 2002) and individual differences in behavioural thresholds can be observed. Hence it is developmentally unlikely that infants are losing

this auditory ability. Furthermore, examination of the presence of mismatch responses, regardless of valence, showed that similar proportions of difference waves (~ 85%) exceeded the baseline confidence interval at both seven and eleven months. Indeed, the interaction between age and electrode group (see Eq. (3) model) shows that the negative shift in the mismatch response with age was smaller for right fronto-central electrodes than left fronto-central electrodes. Such data suggest that we are capturing an ongoing developmental change in the morphology of the mismatch response.

Further, the difference in rise time between the oddball and the standard affected the size of the mismatch response. This is demonstrated by the observed positive two-way interaction between electrode location and rise time difference. Over the FC4 electrode group, when the difference in rise time is larger, and thus the oddball is likely easier to discriminate, the difference wave is more positive. This suggests a sensitivity around FC4 to larger vs smaller rise time differences, with a more pronounced MMR when an oddball is easier to detect. More easily-discriminated stimuli typically elicit larger difference waves in infants (Cone, 2015; Cheour et al., 1998; Sams et al., 1985). As the current infants get older, the difference in responses to larger and smaller changes in rise time around FC4 reverses. This suggests that easy-to-detect changes in rise time elicit a MMN, and more difficult-to-detect changes elicit a more positive MMR. The possibility of the same infant exhibiting an MMR to some stimuli and an MMN to other, more easily discriminated stimuli, fits with prior data from other infant MMN research (Cheng and Lee, 2018).

Regarding the difference between left (FC3) and right (FC4) fronto-central electrode groups, this should be interpreted with caution. Although the broader neural AM literature suggests that rise time processing may differ developmentally between left and right brain regions, the differential responses of the left and right frontotemporal regions reported here could be due to physiological factors affecting how electrophysiological fluctuations are transmitted from the brain to the scalp (Lew et al., 2013; Noreika et al., 2020). The prior auditory neural literature suggests that the right and left hemispheres play different roles in auditory and linguistic processing, with rapid, phonemic-rate transitions processed in the left (Boemio et al., 2005) and slower modulations processed in the right (Sammler et al., 2015). Pre-reading children show this hemispheric specialisation for "syllabic" but not "phonemic" rates of AM SSN (4 vs 80 Hz; Vanvooren et al., 2014), and both children and adults with dyslexia show atypical right hemisphere synchronisation in response to 4 Hz AM noise (Lizarau et al., 2015). Our data are consistent with this literature in that frontocentral electrodes over the right side of the scalp appear more sensitive to differences in rise time than electrodes over the left, however without source localisation we cannot be assured that this is a difference in functional lateralisation.

As noted earlier, rise times play an important mechanistic role in rhythm detection. Amplitude rise times are important for the perception of rhythm because they determine the acoustic experience of "P-centres", the perceptual moment of occurrence ("perceptual centre") of each syllable (or musical beat) for the listener (Morton et al., 1976; Hoequist, 1983). Accurate perception of the beat structure of speech based on P-centres may be important for the temporal prediction of upcoming speech information (Kotz et al., 2009), enabling infants to build a temporal framework related to extraction of the linguistic hierarchy. The current data suggest that the rise time discrimination skills required to construct such a temporal framework are already well-developed by seven months. As rise time is a dynamic measure based on changes reflecting the shape of the sound pressure wave, it cannot be compared in a simple way to other measures in the infant literature used to index temporal processing, such as duration perception or gap detection. For example, infant studies related to rapid auditory processing theory as a mechanism underpinning DLD and dyslexia (Tallal, 1980) have established that by 6 months of age, some infants can detect a gap between two tones that is as short as 70 ms (Hämäläinen et al., 2019). Data from individual tones of this nature are

not comparable to the rise time measure used here. Detection of a silent gap of 70 ms does not mean that the same infant brain should be able to detect an amplitude rise time of 70 ms, as the neural bases of these abilities are quite different.

4.1. Conclusions

The results reported here are unambiguous with respect to infants' ability to detect changes in rise times. Although our stimuli did not challenge infants' detection thresholds, the data reveal greater sensitivity than anticipated from behavioural threshold research (Kalashnikova et al., 2018). Accurate detection of these rise time differences is likely to be important for phonological development, broader language development and the accuracy of neural tracking of the speech envelope (Goswami, 2019, for review). Mechanistically, rise time processing enables the infant brain to represent the amplitude envelope of the highly rhythmic stimulus that is infant-directed speech (Attaheri et al., 2022; Kalashnikova et al., 2018; Leong et al., 2017; Ortiz Barajas et al., 2021). The neural ability to discriminate these amplitude rise time cues revealed here highlights the readiness of the infant brain to process speech rhythm (Mehler et al., 1988). Accordingly, rise time discrimination is likely to support the infant brain in the acquisition of language. The neurophysiological results found here indicate robust processing by infants of this critical acoustic information during the early, pre-verbal stages of language development.

Ethics approval statement

The project from which these results were found was approved by the Psychology Research Ethics Committee of the University of Cambridge, U.K., in accordance with the Declaration of Helsinki.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data are available at https://osf.io/v96xe/.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dcn.2022.101075.

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