



Using fNIRS to examine occipital and temporal responses to stimulus repetition in young infants: Evidence of selective frontal cortex involvement



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ABSTRACT

How does the developing brain respond to recent experience? Repetition suppression (RS) is a robust and well-characterized response of recent experience found, predominantly, in the perceptual cortices of the adult brain. We use functional near-infrared spectroscopy (fNIRS) to investigate how perceptual (temporal and occipital) and frontal cortices in the infant brain respond to auditory and visual stimulus repetitions (spoken words and faces). In Experiment 1, we find strong evidence of repetition suppression in the frontal cortex but only for auditory stimuli. In perceptual cortices, we find only suggestive evidence of auditory RS in the temporal cortex and no evidence of visual RS in any ROI. In Experiments 2 and 3, we replicate and extend these findings. Overall, we provide the first evidence that infant and adult brains respond differently to stimulus repetition. We suggest that the frontal lobe may support the development of RS in perceptual cortices.

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1. Introduction

The past decade has seen dramatic increases in our knowledge about the organization of the developing brain (Aslin et al., 2015). However, the majority of these investigations are targeted at understanding how development occurs in specific domains (e.g., how does the infant brain respond to speech or faces compared to other types of audio or visual stimuli? how do these responses change with development of language or face perception?). As a result, little is known about the basic functional organization of the developing brain especially early in life. To this end, the current study presents the first systematic investigation of the development of one of the most well-established neural phenomena in cognitive neuroscience, repetition suppression.

Repetition suppression (RS) is defined as decreased neural activity in response to repeated presentation of a stimulus. This phenomenon is broadly considered to be “[o]ne of the most robust experience-related cortical dynamics” (Grill-Spector et al., 2006). RS has been thoroughly studied in the adult brain using single-cell recordings, EEG, and fMRI, in human and non-human primates has been documented in response to a wide variety of auditory and visual stimuli (Grill-Spector et al., 2006; Krekelberg et al., 2006; Schacter et al., 2007). While the behavioral correlates or consequences of RS remain under debate, there is evidence that RS is related to a form of implicit memory, repetition priming, or the increased ability to respond to with stimulus repetition (Schacter et al., 2007). Moreover, the phenomenon of RS exhibits a number of parallels with habituation, a widely studied and employed phenomenon in the developmental literature characterized by the reduction in looking time to a repeated stimulus (Turk-Browne et al., 2008). Thus, RS is a robust phenomenon arising from stimulus repetition that may have direct implications for experience-based changes in behavior in both adults and infants.

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1.1. Repetition suppression in the adult brain

In adults, RS is broadly considered a perceptual phenomenon: Perceptually-selective cortices exhibit reductions of activity with the repetition of their preferred sensory input. There is a large literature showing RS to visual stimuli in numerous regions of the visual cortex in adults. Focusing on the fMRI literature, RS has been exhibited to a wide range of stimuli (Sawamura et al., 2005) with particular focus on object-selective cortices such as the lateral occipital cortex or LOC (Cant and Goodale, 2007; Eger et al., 2004, 2008; Grill-Spector et al., 1999). There is also a literature, albeit sparser, showing RS in the temporal cortex of adults to auditory stimuli. Bergerbest et al. (2004) employed environmental (non-speech) sounds and found reductions in neural activity bilaterally in the superior temporal sulcus (STS) for repeated vs. initial presentations of sounds. Employing MEG, Marinkovic et al. (2003) found that repetition of words modulated neural activity in a large bilateral region comprising the STS and additional regions both anterior and posterior to the STS. Similarly, Zevin et al. (2010) found that the temporal cortex was modulated by repeating vs. alternating syllables along different acoustic dimensions (talker, phonemic category).

The phenomenon of RS has been used to map areas of the cortex based on the assumption that regions which show modulation to repetition of the sensory input are highly selective and restricted. With precisely controlled stimuli, this assumption appears borne out. However, repetition-related changes in neural activity frequently extend beyond regions that appear to be specialized for the sensory processing of a given stimulus. For example, RS is found in face-selective regions of the cortex in response to the repetition of a face (Avidan et al., 2002; Rotshtein et al., 2005; Scherf et al., 2011). However, these responses are only selective if the repetition used to produce adaptation is different pictures of the same person and not identical pictures of that person (Rotshtein et al., 2005). A different and much more diffuse pattern is observed if a single picture of a face is used. In this case, RS is found in many lower-level regions as well as more face-selective regions (de Gardelle et al., 2013; Gilaie-Dotan and Malach, 2007; Rotshtein et al., 2005; Scherf et al., 2011). These low-level regions include the middle occipital gyrus and the LOC. Similarly, Sawamura et al. (2005) found that repetition of (non-face) objects modulated activity in all regions that were found to be selective to objects, including V3 and inferior parietal regions (e.g., intraparietal sulcus, IPS). Thus, RS can be a selective phenomenon that can be used to map the cortex, but with simple repetition of a single picture, RS occurs broadly in both low-level sensory and higher level perceptual cortices.

Finally, while RS is often considered a single phenomenon in adults (i.e., one that modulates responses in perceptual cortices), it has been argued that multiple processes might underlie RS. Schacter et al. (2007) reviewed the literature linking repetition suppression with behavioral measure of priming. Notably, they report numerous studies demonstrating that repetition modulates responses in the frontal cortex (specifically the prefrontal cortex) as well as perceptual cortices. Moreover, in general, these studies find the most consistent and robust correlations between neural activity and behavior in the frontal cortices as opposed to the perceptual cortices. For this reason, the authors argue that “there are at least two distinct mechanisms involved in the reductions in activity” in response to stimulus repetition (Schacter et al., 2007, p. 174). One mechanism is perceptual in nature: Perceptual cortices exhibit reductions in neural activity after repetition because of a sharpening of underlying representations (consistent with Grill-Spector et al., 2006). The other mechanism “primarily reflects changes in the prefrontal cortex [and these changes] drive behavioral priming effects in a top-down manner” (Schacter et al., 2007, p. 174).

1.2. Repetition suppression in the developing brain

While numerous studies have examined neural responses in infants to auditory and visual stimuli (for a recent review see Aslin et al., 2015), little is known about how the young brain responds to the repetition of this sensory information. Studies examining infant neural responses to simple auditory and visual stimuli have largely found similar profiles of responses compared to what has been found in adults: Visual stimuli elicit responses in the occipital cortex (Taga et al., 2003, 2004); auditory stimuli elicit responses in the temporal cortex (Nakano et al., 2008; Taga and Asakawa, 2007). Building on these seminal but largely confirmatory findings about the infant brain, a crucial next step is to examine basic perceptual cortex responses to stimulus repetition. As reviewed above, RS is a basic and well-established phenomenon in the adult fMRI literature. Indeed, many of the candidate theories of the specific mechanisms that would give rise to RS (neural fatigue, representational sharpening and facilitation, Grill-Spector et al., 2006) are grounded in principals of cortical/neural function and therefore would likely be present early in life. In other words, from these theories, RS is a conserved and basic property of the cortex and should readily be a property of the infant brain. Indeed, Sawamura et al. (2005) found that visual RS is strikingly similar across human adults and non-human primates, again suggesting that RS should also be shared between infant and adult humans.

Very few previous studies have examined repetition-related neural phenomena in the developing brain, and no study has systematically investigated repetition suppression across multiple types or modalities of stimuli. In order to make spatial inferences about RS, we focus on papers employing functional near-infrared spectroscopy (fNIRS, see reviews of this method by Gervain et al., 2011; Lloyd-Fox et al., 2010) and fMRI as these neuroimaging methods allow for robust spatial inferences (see Nordt et al., 2016, for review of RS in developmental populations using ERP and MEG studies). Two studies have examined effects of repetition on auditory stimuli in infancy. Nakano et al. (2009) recorded responses in the temporal and frontal cortices to repetition of simple speech stimuli (e.g., “ba” vs. “pa”). The authors report a significant reduction in response across many repetitions of a single token broadly across both the temporal and frontal cortices but only a recovery of response in the prefrontal cortex. Dehaene-Lambertz et al. (2006) examined effects of repetition of sentences on 3 month old infants in an fMRI study. Though speech seems to elicit responses in the temporal cortices bilaterally, sentence repetition results in repetition enhancement in the frontal cortex only. Thus, across two studies of auditory stimuli in young infants, there appears to be an effect of repetition in the frontal cortex though with different directions of effects (repetition suppression vs. repetition enhancement). Studies from two groups have examined effects of repetition using visual stimuli, however, this work was designed to control for visual repetition and examine more specialized cortical responses. Southgate et al. (2014) presented infants with two repeats of videos where an action was being depicted which was followed either by a repetition of the same goal or a new goal. While their goal was not to examine visual repetition suppression per se, the authors present evidence for RS to displays depicting goal-directed behavior in the IPS and provide some initial evidence that the infant brain can exhibit RS similarly to adults. Similarly, Hyde et al. (2011) examined effects of repetition of visual displays of number but the authors controlled for low-level visual differences. Again, the authors find a similar profile of response as adults (i.e., reductions of response in the parietal cortex selectively). Thus, these studies don’t reveal how the developing brain responds to repetition of visual stimuli per se. For example, it is not known whether the repetition of visual stimuli might result in modulation of the frontal cortex similar to the two studies previously reported with auditory stimuli in infants.

We employed functional near-infrared spectroscopy (fNIRS) to record neural activity in young infants (5–7 months) to examine the effects of repetition in the developing brain. Specifically, we compared responses in frontal, temporal and occipital cortices to the repetition of auditory and visual stimuli. Importantly, we employed MR-coregistration of our fNIRS recordings to provide precise neuroanatomical localization of the neural recordings. Stimuli were presented in either a Repeated block (a single stimulus presented 8 times) or a Variable block (8 different stimuli). Importantly, these blocks are presented in randomized order to disentangle the general effects of experimental habituation or fatigue from the responses to stimulus repetition. If the infant brain has a similar response to repetition as the adult brain, we expect to find that infants would exhibit RS, an attenuation of neural activity, during Repeated blocks in the corresponding perceptual cortex (e.g., the occipital cortex would exhibit an attenuated response to Repeated blocks of visual stimuli compared to Variable blocks). Finally, we investigated auditory and visual stimuli that vary along many perceptual dimensions (i.e., to drive repetition suppression broadly in both the auditory and visual systems) but are engaging to infants (i.e., to maintain their attention throughout the experiment). To this end, we presented infants with familiar words (e.g., “doggie”) and smiling faces from a diverse group of people.

2. Experiment 1: auditory and visual repetition suppression in the infant brain

2.1. Methods

2.1.1. Participants

Eighteen (18) participants were included in the analysis of Experiment 1, ages 5–7 months ($M = 5.8$, $SD = 0.6$, $Min = 5.2$, $Max = 7.0$ months); 9 female and 9 male. Of the included infants, 88.9% heard only English at home. Two other participants heard another language from their family 60 or 90% of the time. Participants were identified as 88.9% Caucasian; 1 was identified as black. Two were identified as Hispanic with the remainder identified as non-hispanic. Infants who were tested could be excluded from subsequent analyses for three reasons defined a priori: (1) for not looking for at least three blocks in all four conditions (12 blocks total), (2) for excessive noise in the signal as determined by visual inspection, usually coinciding with fussiness, poor cap fit, or excess hair or (3) if their average response to any condition was a significant outlier ($\pm 2SD$). Eight additional participants were excluded based on these criteria – 7 for noisy recordings and one for fussiness and refusal to wear the NIRS cap.

2.1.2. Materials and experimental design

The experiment was conducted in a darkened room. During the experiment, the infant sat on a caretaker's lap surrounded by a black curtain to reduce visual distraction and separate the participant from the experimenter. Infants watched a video with 32 blocks of stimuli: Sixteen audio blocks and 16 visual blocks. Half of each type of block contained 1 stimulus presented 8 times (Repeated condition) and the other half contained 8 different stimuli presented once (Variable condition). The same set of stimuli was used in both the Repeated and the Variable conditions. All stimuli had a stimulus onset asynchrony of 1 s. The inter-stimulus interval for visual stimuli was always 25 s. The ISI for audio stimuli ranged from 7 to 8 s. The audio stimuli were 8 common words familiar to infants (apple, baby, bottle, blanket, cookie, diaper, doggie, story). Words were spoken with a local accent for Rochester, NY using an infant-directed speech register. The visual stimuli were 8 smiling faces from the NimStim database (Tottenham et al., 2009). Faces were chosen, including males and females (equal frequency) of

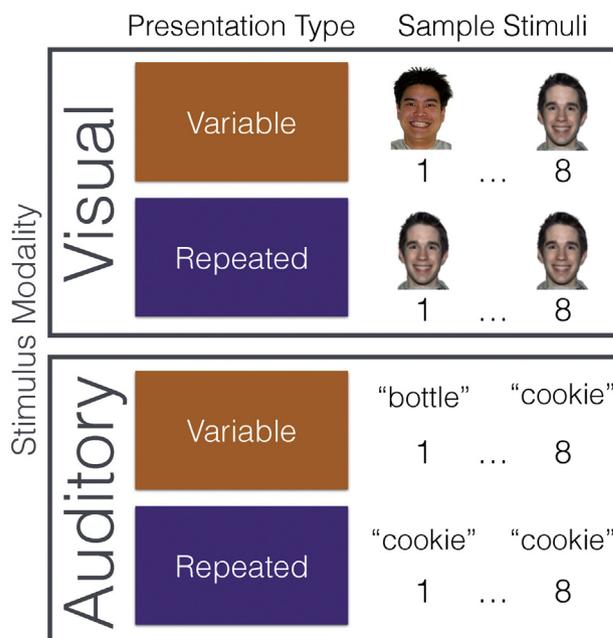


Fig. 1. Illustration of the experimental design. There are 4 types of stimulus blocks in the current study: Auditory Variable, Auditory Repeated, Visual Variable, Visual Repeated. These blocks vary along two dimensions: Stimulus Modality and Presentation Type. Stimulus modality is either visual or auditory blocks which differ in the type of stimuli employed (8 smiling faces and 8 familiar words spoken in infant-directed speech, respectively). Presentation Type corresponds to whether all 8 of these stimuli are presented in random order or whether a single stimulus is repeated 8 times: Variable and Repeated blocks, respectively.

multiple races and ethnicities, in order to increase the likelihood of visual discrimination of each individual through low-level visual differences such as color, luminance, and spatial frequency.

All four block conditions (Visual Repeated, Visual Variable, Auditory Repeated, Auditory Variable) were presented in shuffled order. The same stimuli were used for both the Repeated and Variable conditions. Each of the Variable blocks presented all 8 stimuli in a shuffled order, and each of the Repeated blocks employed one of these 8 stimuli (not yet employed in a previous Repeated block but presented in each Variable block). This design controlled for the relative exposure or familiarity that infants had with each stimulus. See Fig. 1 for a visualization of the experimental design and stimuli.

In between blocks, a baseline video was presented with dim fireworks on the screen and soft music (length was pre-determined and randomly selected to be between 4 and 9 s). Note that under ideal circumstances, the baseline should contain neither auditory nor visual stimuli. However, it is not possible to maintain infants' attention and avoid their tendency to become fussy in the absence of any stimulation. Thus, the low-salience fireworks and music displays served as a minimally salient inter-block baseline. To control for cross-modal (auditory–visual) activation, during the audio blocks, the fireworks video continued to play on the screen, and during the visual blocks, the music continued to play in the background. Thus, all blocks contained cross-modal sensory input with the cross-modal input being the same as that employed in the baseline (e.g., for the visual blocks, the same calm, soft music as the baseline was played). Participants watched the video display until they stopped looking consistently or all experimental blocks were viewed.

2.1.3. fNIRS recordings

fNIRS recordings were collected using a Hitachi ETG-4000. Twenty-four channels were used in the NIRS cap, with 12 over the back of the head to record bilaterally from the occipital lobe, and 12

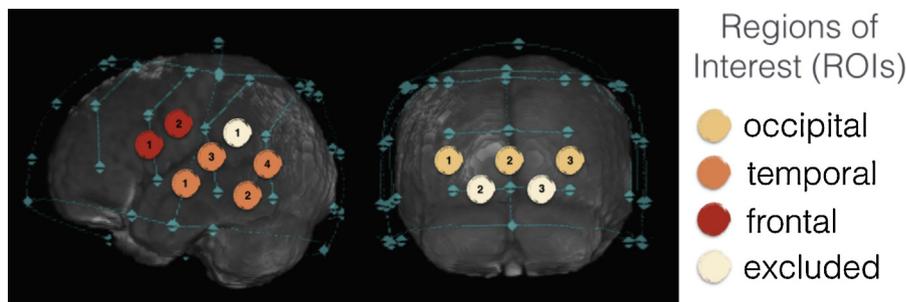


Fig. 2. NIRS holder reconstruction for an illustrative infant. Circles represent locations of the 12 channels with consistently good optical contact across the population recruited that were included in the MR coregistration analysis. Circles are colored according to their regions of interest (ROIs) and numbers indicate the specific channel as listed in Table 1).

over the left side of the head to record from the left temporal lobe. The channels were organized in two 3x3 arrays, and the cap was placed so that, for the lateral array, the central optode on the most ventral row was centered over the left ear and, for the rear array, the central optode on the most ventral row was centered between the ears and over theinion. This cap position was chosen based on which NIRS channels were most likely to record from temporal and occipital cortex in infants. Due to curvature of the infant head, a number of channels did not provide consistently good optical contact across infants (the most dorsal channels for each pad). We did not consider the recordings from these channels in subsequent analyses and only considered a subset of the channels (7 for the lateral pad over the ear and 5 for the pad at the rear array). Caretakers were instructed to refrain from influencing their children, only providing comfort if needed and to keep their children from either grabbing at the cap or rubbing their head against the caregiver.

In order to provide clear, quantifiable anatomical localizations for our fNIRS recordings, we followed the methods reported in Lloyd-Fox et al. (2014) to co-register the fNIRS recordings for the infants with MR-templates. For a full description of these methods see the Supplementary Materials (Beauchamp et al., 2011; Cui et al., 2011; Fillmore et al., 2015; Hammers et al., 2003; Heckemann et al., 2006; Richards et al., 2016; Richards and Xie, 2015; Shattuck et al., 2008).

2.1.4. fNIRS pre-processing

fNIRS recordings were collected at 10 Hz (every 100 ms). The raw data were exported from the Hitachi ETG-4000 to MATLAB (version 2006a for PC) for subsequent analyses with HomER 1 (Hemodynamic Evoked Response NIRS data analysis GUI, version 4.0.0) for a standard preprocessing of the NIRS data. First, the “raw intensity data [was] normalized to provide a relative (percent) change by dividing the mean of the data” (HomER 1.0 manual) and then it was low-pass (cutoff 3 Hz) to remove high frequency noise such as cardiac signals. Second, changes in optical density were calculated for each wavelength, and a PCA analysis was employed to remove motion artifacts. Finally, the modified Beer-Lambert law was used to determine the changes (delta) concentration of oxygenated and deoxygenated hemoglobin for each channel (the DOT.data.dConc output variable was used for subsequent analyses, see the HomER Users Guide for full details, Huppert et al., 2009).

Subsequent analyses were conducted in MATLAB (version R2015b) with custom analysis scripts. These analyses consisted of (1) excluding trials where the experiment was terminated before 14.5 s after the start of the trial; this length of time represents the average time from the start of the trial to the end of the jittered ISI (block duration is 8 s with an average ISI of 6.5 s and a range of 4–9 s). Note: infant looking was closely monitored for the

duration of the study by a researcher. If an infant was not watching the screen for the vast majority of the blocks, the experiment was immediately ended. Thus, we assume a high-proportion of attended stimuli for each of the blocks; (2) calculating the number of trials for each infant for each condition to determine if the infant reached the inclusion criteria of watching a minimum of 3 complete trials per condition; (3) determining the average and variability (standard deviation) concentration of oxygenated and deoxygenated hemoglobin per channel for each condition for each infant; (4) determining the average and variance of oxygenated and deoxygenated hemoglobin within each ROI for each infant; (5) summing the change in concentration of oxygenated hemoglobin between 6 and 14.5 s after block onset for each ROI for each infant; and (6) determining the average change in oxygenated and deoxygenated hemoglobin for each channel and ROI at the group-level (i.e., across infants).

2.1.5. Defining anatomical ROIs using MR-coregistration results

Twenty-seven infants met the criteria (out of 33 from Experiments 1 and 2) for the MR-coregistration analysis (see Fig. 2). For these infants, NIRS channels were co-registered to both an average MR template and an MR of an individual infant contained within the database. Both the average and the individual MR were selected based on age and head size of the infant in the NIRS study. See Supplementary material for more details on MR-coregistration methods.

Based on the channel co-registration results (Table 1), we created 3 anatomical ROIs corresponding to the temporal, occipital and frontal regions. Fig. 3 presents a visualization of the ROIs superimposed on an average infant MRI which weights the color based on the density of recordings over the sample of infants. While we considered all channels within in ROI to be equivalent, not all cortical sub-areas of this region are sampled equally in this ROI. For the temporal ROI (as co-registered to the average MR), there were three major loci of localization within the temporal lobe: The posterior temporal gyrus (59%), the superior temporal gyrus (25%) and the medial and inferior temporal gyri (12%). For the individual MRs and the temporal ROI, the localization was similar but more evenly distributed: The medial and inferior temporal gyri (27%), the superior temporal gyrus (38%) and the middle temporal gyrus (35%). For the occipital ROI and the average MR, channels were predominantly localized to the lateral remainder of the occipital lobe (86%) which delineates regions that do not include the cuneus (6%) and the lingual gyrus (7%). For the individual MR, again the majority of the ROI is localized to the lateral remainder of the occipital lobe (64%) along with the cuneus (15%, lingual gyrus 2%). Finally, for the frontal ROI, using the average MR, the channels primarily localized to the left inferior frontal gyrus (43%) with secondary localization to the precentral gyrus (31%). For the individual MRs, again the

Table 1
Localization of NIRS channels from the Lobar atlas.

Channel no.	MR type	Localization				
		Temporal	Occipital	Frontal	Parietal	Cerebellum
Temporal-1 ^a	Average	100%	0%	0%	0%	0%
	Individual	96%	0%	4%	0%	0%
Temporal-2	average	96%	0%	0%	0%	4%
	Individual	96%	0%	4%	0%	0%
Temporal-3	average	96%	0%	4%	0%	0%
	Individual	63%	0%	26%	11%	0%
Temporal-4	average	96%	0%	0%	4%	0%
	Individual	85%	0%	0%	15%	0%
Occipital-1	average	0%	93%	0%	7% ^b	0%
	Individual	4%	89%	0%	7%	0%
Occipital-2	average	0%	100%	0%	0%	0%
	Individual	0%	100%	0%	0%	0%
Occipital-3	average	0%	85%	0%	15%	0%
	Individual	0%	89%	0%	11%	0%
Frontal-1	average	11%	0%	89%	0%	0%
	Individual	4%	0%	96%	0%	0%
Frontal-2	average	0%	0%	70%	30%	0%
	Individual	11%	0%	11%	70%	0%
Excluded-1	average	40%	0%	0%	59%	0%
	Individual	21%	0%	9%	70%	0%
Excluded-2	average	0%	63%	0%	7%	30%
	Individual	0%	70%	0%	4%	22%
Excluded-3	average	0%	44%	0%	0%	56%
	Individual	4%	63%	0%	4%	26%

Bold values mark the correspondence between a given ROI (e.g., temporal) and the localization to that neuroanatomical region of the brain.

^a See Fig. 2 for a depiction of the location of these channels on the holder.

^b All 'parietal' localizations in this ROI localize to the lateral occipital cortex (LOC) or middle occipital in the other atlases.

These regions are on border of occipital and parietal lobes but broadly considered as a cortical region involved in visual processing. Thus, these localization to parietal are considered functionally equivalent to occipital in relation to the goal of determining a visual/occipital ROI.

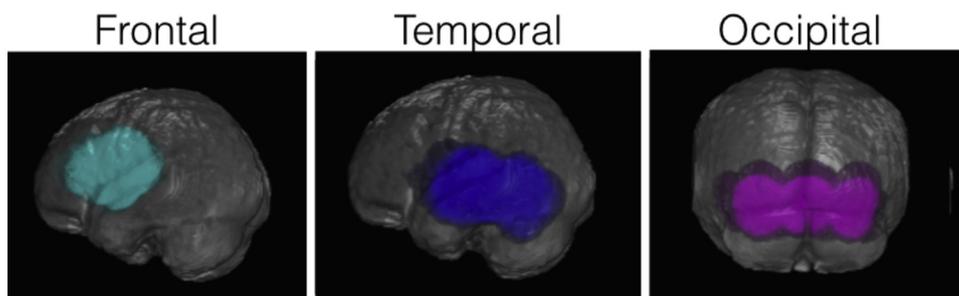


Fig. 3. The three anatomically-defined regions of interest (ROIs) employed in Experiments 1 and 2. Plots are reconstructions of the fNIRS recordings by taking the localization of the center of the channel and adding a 1.5 cm sphere around that center point and weighting these recordings over the population of infants co-registered to this MR template.

primary localization was to the left inferior frontal gyrus (37%), then the precentral gyrus (33%) and the middle frontal gyrus (20%).

2.1.6. Statistical analyses

Analyses are based upon the 3 anatomical ROIs defined based on MR-coregistration of NIRS results. All channels within a ROI were treated equivalently: Activity was simply averaged across all channels within an ROI, then across blocks (3–8 depending on looking time) for each infant. We focused on changes in blood oxygenation rather than deoxygenation as it is most commonly employed in the literature and most robust for infants (Aslin et al., 2015). Three hypothesis-motivated analyses were conducted on averaged responses to provide convergent evidence for the presence of repetition suppression in the infant brain (all within-subjects variables): (1) Comparing activity to baseline (one-sample *t*-test) to discern the individual pattern of activity for each ROI for each block type, (2) Directly comparing Repeated and Variable conditions within a stimulus modality and specifically examining whether there is a reduction of neural activity for repeated stimuli

compared to Variable stimuli (one-tailed paired *t*-test¹), and (3) Direct comparisons of stimulus modality across Variable and Repeated blocks for each anatomical ROI (2×2 ANOVA with stimulus modality and condition). In addition, we examined the time-course of the response and directly compared responses across Variable and Repeated stimulus conditions (one-tailed paired *t*-test) in 1 s bins starting at 4 s after stimulus onset (i.e., averaged response from 4.1 to 5.0 s after stimulus onset was compared across Variable and Repeated conditions to examine whether there was an attenuation of response for Repeated conditions, responses were then compared from 5.1 to 6.0 s and so on).

¹ It is essential to note that this experiment has a very strong and specific hypothesis about the direction of difference between conditions: Evidence of repetition suppression will be only true if there is greater activity for the Variable condition compared to the Repeated condition. Indeed, if we had found repetition enhancement (i.e., increased neural activity for Repeated condition compared to Variable), we would have had to conduct additional experiments to clarify and replication such an unexpected result. Thus, a one-tailed *t*-test is a suitable statistical test here.

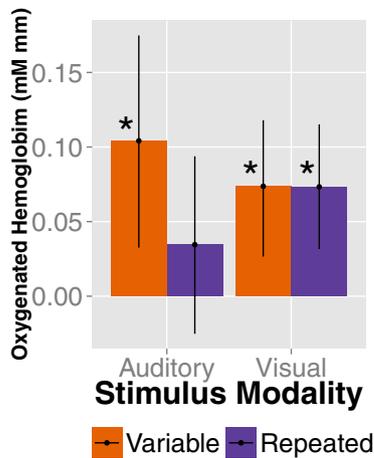


Fig. 4. Responses (averaged from 6 to 14.5 s) of the temporal ROIs to auditory stimuli and the occipital ROIs to visual stimuli are presented. Error bars indicate the standard error of the mean. See Fig. S3 for cross-modal responses (e.g., visual responses in the temporal ROI). Note: each panel presents results from different ROIs.

2.2. Results

Infants included in the final analysis watched each condition an average of 5.5 times (SD = 1.06) for a total of 22 blocks (SD = 4.26).

2.2.1. Effects of auditory repetition in the temporal cortex

The left side of Fig. 4 presents averaged responses for the temporal lobe to auditory stimuli. Comparing responses to auditory stimuli in the temporal cortex to baseline, we find a significant increase in blood oxygenation in the temporal channels to the Variable Auditory condition ($t(17) = 2.55, p = 0.02$) and no significant response to the Repeated Auditory condition ($t(17) = 1.50, p = 0.15$). By comparison, responses in this ROI are not significant to visual stimuli in either condition ($ts(17) < 1.4, ps > 0.15$). While this provides suggestive evidence of auditory repetition suppression in the temporal cortex, a direct comparison of the summed responses between the Repeated and Variable conditions is not significant, $t(14) = 1.23, p = 0.12$. Finally, an ANOVA comparing responses in this ROI to auditory and visual stimuli across both stimulus conditions revealed no main effects nor an interaction ($Fs(1,17) < 1.8, ps > 0.2$). See Fig. S3 for cross-modal responses. Time-course analyses revealed reliable differences between Auditory Variable and Repeated stimuli starting at 10 s after stimulus onset (Fig. 5: 10–11 s: $t(17) = 1.41, p = 0.089$; 11–12 s: $t(17) = 1.95, p = 0.034$; 12–13 s: $t(17) = 1.55, p = 0.070$). Thus, two tests suggested the presence of auditory repetition suppression in the temporal lobe of young infants: Looking at the averaged response, we find a robust response is restricted to Variable Auditory stimuli. This provides some indirect evidence of repetition suppression but the two direct and planned comparisons between Variable and Repeated stimuli using the averaged response were not significant. Time-course analyses directly compared responses to Variable and Repeated auditory stimuli and found reliable differences for 3 time windows. Taken together, these results are suggestive of auditory repetition suppression in the temporal lobe.

2.2.2. Effects of visual repetition in the occipital cortex

Neural responses look markedly different in occipital cortex to visual stimuli. Specifically, we find highly similar responses to both the Variable and Repeated conditions. Averaged responses are robustly greater than baseline for both Variable and Repeated conditions ($ts > 3.15, ps < 0.0059$, Fig. 4) and, unsurprisingly, the response to the Variable stimuli is not significantly greater than

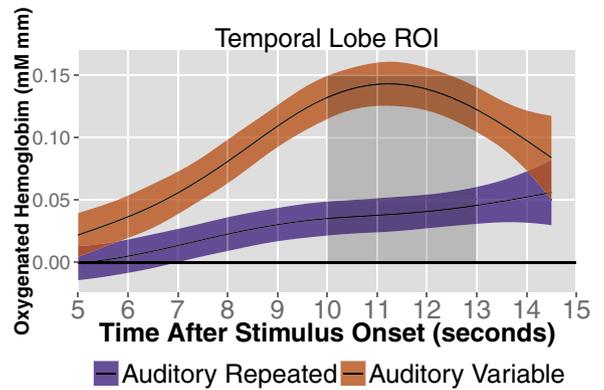


Fig. 5. Time-course of response in the temporal ROI to Auditory Variable and Repeated stimuli. Responses are smoothed based on a general linear model (stat.smooth in R) based on average responses for each infant. Shaded region of the graph indicates periods of time where the response is greater for variable than repeated.

the response to the Repeated stimulus ($p = 0.5$). An ANOVA comparing stimulus type (auditory and visual) and condition (repeated and variable) found no main effects or interactions ($Fs(1,17) < 2.75, ps > 0.11$). Turning to the time-course analyses, there were no time windows where the variable visual condition was greater than the repeated visual condition ($ts(17) < 1.1, ps > 0.14$, Fig. 6). Thus, unlike the auditory responses in the temporal cortex, there is no indication of visual repetition suppression in the occipital cortex. See Fig. S3.

2.2.3. Frontal cortex responses to auditory and visual repetition

The same analyses were conducted with the frontal ROI as with the modality-specific perceptual cortices. Comparisons of average responses to baseline revealed a robust response for Variable auditory stimuli only ($t(17) = 4.41, p < 0.001$; all others, $ps > 0.1$, Fig. 7). Comparing responses in this ROI within stimulus modality indicated that responses to Variable auditory stimuli was significantly greater than Repeated auditory stimuli ($t(17) = 1.85, p = 0.041$) but not for visual stimuli ($p = 0.94$). Moreover, an ANOVA comparing stimulus modality and presentation condition revealed a significant interaction between stimulus modality and condition ($F(1,17) = 6.55, p = 0.020$), a marginally significant difference between stimulus modality indicating greater responses in this region to auditory than visual stimuli ($F(1,17) = 3.14, p = 0.094$) and no main effect of condition ($p = 0.9$). This pattern of results supports the presence of a repetition suppression response for auditory stimuli in the frontal cortex but not visual stimuli.

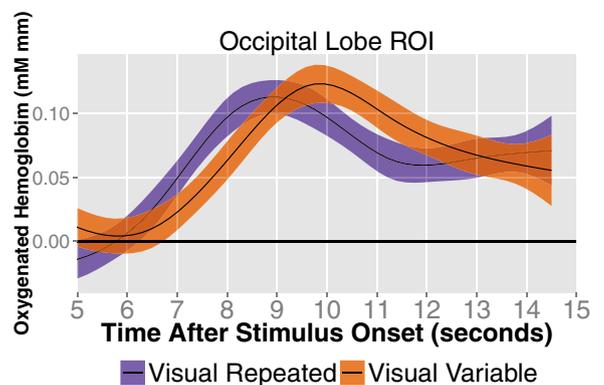


Fig. 6. Time-course of response in the occipital ROI to Visual Variable and Repeated stimuli. Responses are smoothed based on a general linear model (stat.smooth in R) based on average responses for each infant. Shaded region of the graph indicates periods of time where the response is greater for variable than repeated.

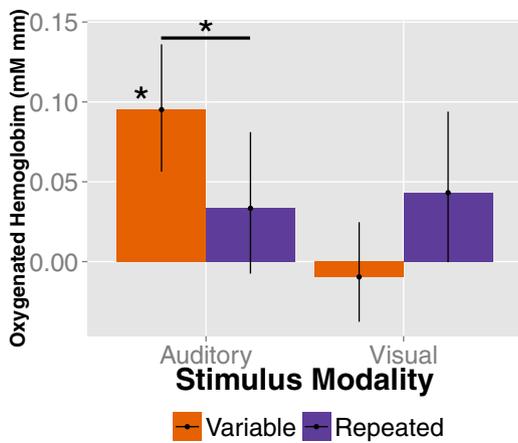


Fig. 7. Responses of the frontal cortex to auditory and visual stimuli. Error bars indicate the standard error of the mean.

Turning to the time-course analyses (Fig. 8), the response to Auditory Variable stimuli is greater than Auditory Repeated for a number of time windows (8–9 s: $t(17) = 1.51, p = 0.075$; 9–10 s: $t(17) = 2.28, p = 0.018$; 10–11 s: $t(17) = 2.17, p = 0.022$; 11–12 s: $t(17) = 1.30, p = 0.11$; 12–13 s: $t(17) = 2.17, p = 0.022$; 13–14 s: $t(17) = 1.63, p = 0.061$, see shaded regions of Fig. 8a). In contrast, there is no time window in which Visual Variable responses are greater than Visual Repeated ($ps > 0.67$, see Fig. 8b). Indeed, from visual inspection, the pattern of response is more consistent with repetition enhancement for visual stimuli in the frontal lobe.

2.3. Discussion

In a direct comparison of stimulus modality (auditory and visual stimuli) and repetition in the infant brain, we report important dissociations between perceptual-cortex responses to repetition and frontal cortex responses. Specifically, we see some suggestion of auditory repetition suppression in auditory selective cortex (temporal lobe) but no suggestion of visual repetition suppression in the occipital lobe. It is unlikely that the lack of visual repetition suppression is being driven by the heterogeneous faces employed. While the current age being tested (6 months) is before many of the well-documented face narrowing and other-race effects (Kelly et al., 2007), previous work has established that infants exhibit preferences for female faces (compared to male faces) within their own ethnicity by 3 months (Quinn et al., 2008). However, it is unlikely that differential neural activation for male vs. female faces is boosting neural responses in the repeated condition. Carlsson et al. (2008) used fNIRS to examine 6 month old, neural responses

to maternal and novel female faces (an analogous situation to male vs. female faces). They found increased activity to maternal faces. This is the opposite direction that would be expected if responses to novel stimuli boosted occipital responses. Moreover, these increases responses to maternal faces were found in the right temporal-frontal regions of the brain.

In addition to the findings in the temporal and occipital lobes, we find differences in frontal lobe responses to repetition across auditory and visual stimulus types. Specifically, there is robust evidence for auditory RS in the frontal lobe but no evidence of visual RS (even some indication of repetition enhancement). Thus, we report two unanticipated findings: (1) the absence of an attenuated neural response to visual repetition, and (2) differential involvement of the frontal lobe in repetition across perceptual modalities. We follow-up on both of these findings in our two subsequent experiments.

3. Experiment 2: replication and extension of visual repetition suppression findings

In Experiment 2, we focus on the surprising absence of visual repetition suppression with the goals of replicating and then extending this finding. First, we conducted a straight-forward replication of Experiment 1 by recording with the same stimuli and the same cortical regions. Our predictions are to find a lack of repetition suppression to faces in the occipital lobe and evidence of either no repetition suppression or repetition enhancement in the frontal lobe. Second, we investigated whether these findings are a result of the use of faces as our stimuli. While studies with adults strongly suggest that repeating identical pictures of faces will result in RS in many visual regions that are accessible to our fNIRS recordings (de Gardelle et al., 2013; Gilaie-Dotan and Malach, 2007; Rotshtein et al., 2005; Scherf et al., 2011), not just face-selective regions such as the FFA that would not be accessible with our recordings, it could be that we can find evidence of visual RS with the use of other visual stimuli. To that end, we introduce corresponding repeated and variable blocks of visual stimuli using fruit instead of faces. Fruit are a contrast to faces in a number of ways: They are non-social and do not exhibit specialized visual processing and have greater lower level visual differences between the stimuli. Third, we introduce a new type of block that will increase the amount of repetition of a single face. Specifically, we introduce a new face to the face stimulus set and select one of these (now 9) faces to be repeated in blocks throughout the experiment. Infants will see this face between 24 and 64 times throughout the experiment. Increasing repetition for a single face will achieve two ends. First, because we find robust occipital lobe responses to both Repeated and Variable Face stimuli in Experiment 1, it is possible that we did not see

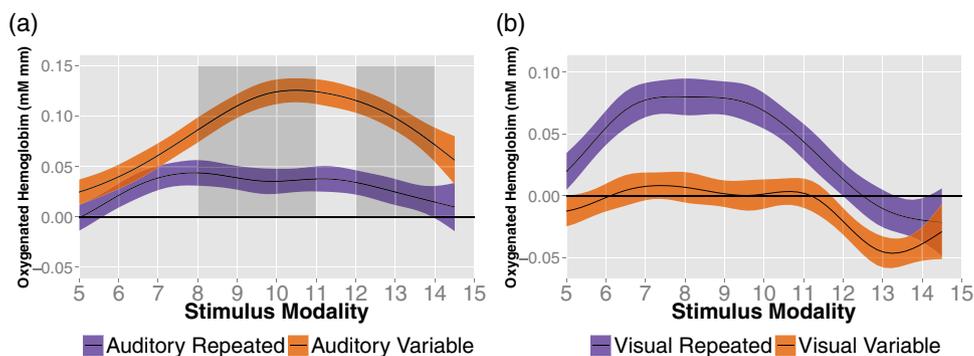


Fig. 8. Time-course of response in the frontal ROI to auditory and visual stimuli in both variable and repeated conditions. Responses are smoothed based on a general linear model (stat.smooth in R) based on average responses for each infant. Shaded region of the graph indicates periods of time where the response is greater for variable than repeated.

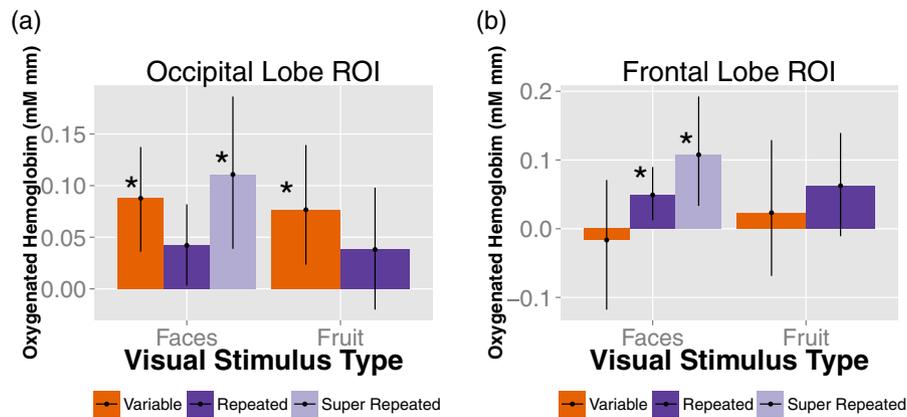


Fig. 9. Responses (averaged from 6 to 14.5 s) to two different types of visual stimuli: (a) Faces and (b) fruit. Error bars indicate the standard error of the mean.

repetition suppression because the faces are more interesting to infants or are more complex than the spoken words. If either of these were true, it could require more repetition of a single face before it's response is suppressed. Second, by introducing a **Super Repeated** condition, we will be able to determine whether simply increasing repetition of a face will result in visual repetition suppression in the occipital ROIs. Moreover, by increasing repetition for one condition, we can better test whether the infant frontal lobe is responding to visual stimuli with repetition enhancement. If this is the case, the prediction is that the frontal lobe will exhibit the strongest response to the Super Repeated condition.

3.1. Methods

3.1.1. Participants

Fifteen participants were included in the analysis of Experiment 2, aged 5 to 7 months old ($M = 6.0$, $SD = 0.6$, $Min = 5.2$, $Max = 7$ months); 9 female and 6 male. Of these participants, 73.3% heard only English at home. The other participants heard another language from their family no more than 15% of the time. Participants were identified as 73% (11/15) Caucasian only; 1 identified as Hispanic; 3 identified as multiracial. Eight participants were excluded for the same criteria as the previous experiment; 5 not looking; 2 noise; 1 outlier.

3.1.2. Materials and procedure

The total number of blocks was increased from 32 to 40, with only visual conditions; no auditory blocks were included. As with the previous experiment, we included eight Variable Faces blocks and eight Repeated Faces blocks. We used the same set of faces as in Experiment 1 but adding a ninth face to create a Super Repeated Face condition. In this condition, the ninth face in the set (particular faces were randomized across subjects) was presented in eight Repeated blocks in order to examine whether greater exposure to a single face would reduce occipital responses. We also introduced a set of visual stimuli that were not faces and presented these eight stimuli in both Repeated and Variable blocks using the same method as for the faces in the previous two experiments. This introduced Repeated Fruits (1 fruit presented 8 times) and Variable Fruits (8 fruits presented in shuffled order) blocks to the experiment. The same baseline video was used, and the music played during all blocks. Otherwise, the procedure was identical to Experiment 1. Given that the first Super Repeated Face block is identical to a Repeated face block (the first repetition of a given face), the first Super-Repeated face block was considered part of the Repeated face condition.

3.2. Results

Experiment 2 had five conditions and only presented visual stimuli, whereas Experiment 1 had four conditions (2 visual and 2 auditory). However, the infants included in the final analysis watched a comparable number of repetitions of each condition: average of 4.85 repetitions per condition ($SD = 1.84$) and a total of 24.3 blocks ($SD = 9.2$).

3.2.1. Replication of Experiment 1: Repeated vs. Variable Face presentation

We presented a new group of infants the same two visual conditions as Experiment 1 (faces in Repeated and Variable blocks). Focusing on occipital and frontal anatomical ROI results for those two conditions only, we find broadly convergent patterns with Experiment 1 (Fig. 9). Comparing responses to baseline, there is a robust response of the occipital lobe to the Variable Face condition ($t(14) = 3.47$, $p = 0.0038$) and a marginally significant increase to the Repeated Face condition ($t(14) = 1.93$, $p = 0.075$). There is a marginally significant decrease in activity for Repeated compared to Variable Faces ($t(14) = 1.44$, $p = 0.086$). However, comparing the time-course of responses, there are only two time-windows with any indication of increased activity to variable compared to repeated face presentation (8–9 s: $t(14) = 1.75$, $p = 0.051$; 9–10 s: $t(14) = 1.77$, $p = 0.050$, see Fig. S4). Thus, while we find some indication of increased activity to Variable compared to Repeated Face presentation, there is still no robust evidence of visual repetition suppression in the occipital lobe in infants.

Turning to the frontal lobe responses, we find patterns consistent with Experiment 1 (see Fig. 9). Specifically, we again do not find evidence for repetition suppression in the frontal lobe to visual stimuli. We also see some suggestion of repetition enhancement. First, comparing responses to baseline, we find a robust response for Repeated Faces ($t(14) = 2.39$, $p = 0.032$) but not for the Variable Face condition ($p = 0.76$). However, we find no significant difference between the two conditions (one-tailed t -test examining whether repeated response is greater than variable response, $t(14) = 1.21$, $p = 0.12$). Comparing the time-course of responses, there is a significant increase in activity to Repeated over Variable Face presentation only in the last time-window ($t(14) = -1.85$, $p = 0.043$, see Fig. S4). We continue this line of investigation later in this section as we consider responses to the Super Repeated condition.

3.2.2. Extension to new visual stimuli: fruit

We now consider whether these same patterns are evident for the visual presentation of another type of stimuli, distinct from faces: Fruit. Broadly, we find the same patterns of activity in both

the occipital and frontal ROIs for both types of visual stimuli (see Fig. 9). Starting with the occipital lobe, there is a robust increase from baseline in the Variable Fruit condition ($t(14) = 2.58, p = 0.022$) but not the Repeated Fruit condition ($p = 0.23$). However, we find no significant difference in response across these presentation types ($p = 0.20$). Comparing responses in a two-way repeated measure ANOVA, we find no main effects of stimulus type ($p = 0.77$) nor an interaction between stimulus and presentation type ($p = 0.91$) but there is a marginally significant main effect of presentation type ($F(1,14) = 3.07, p = 0.1$), suggesting a greater response to Variable presentation for both types of visual stimuli.

Turning to the frontal lobe, we find no significant response to either fruit condition (Variable or Repeated, $ps > 0.14$) nor any evidence for increased response to the Variable Fruit condition ($p = 0.21$). Similarly, in comparing the time-course of the response, there is only a single time window with a significant increase in activity for Repeated vs. Variable Fruit stimuli (6–7 s: $t(14) = -1.76, p = 0.050$, see Fig. S4). Thus, while we continue to find no evidence for repetition suppression to visual stimuli in the frontal lobe, we do not find any suggestion of repetition enhancement for fruit stimuli.

3.2.3. Effects of increasing visual repetition

Finally, we consider the responses of the occipital and frontal ROI to increased repetition of face stimuli (Super repeated conditions in Fig. 9). In the occipital lobe, there is a robust response to the super repeated face condition ($t(14) = 2.82, p = 0.014$), and this response is not significantly reduced from the variable presentation of faces ($p = 0.68$). Using a repeated measure ANOVA to compare responses across the three types of face presentation reveals no difference across presentation type ($p = 0.26$). Thus, we find that simply increasing the repetition of a single face does not result in a suppression of the occipital lobe to this stimulus. Instead, numerically, the response in this region trends towards repetition enhancement for this condition.

In the frontal lobe, we also find a robust response to the super repeated face condition ($t(14) = 2.53, p = 0.024$) and, numerically, this is the highest response for the frontal lobe. But a direct comparison between presentation conditions using a repeated measures ANOVA does not reveal any significant differences across presentation type ($p = 0.14$). Thus, we again find no evidence of repetition suppression for visual stimuli in the frontal lobe, and while there is some suggestion that the frontal lobe exhibits repetition enhancement for visual stimuli, these effects are not statistically robust (see Fig. S4 for time-course figures).

3.3. Discussion

The results of Experiment 2 largely confirm the findings concerning occipital cortex responses to visual repetition from Experiment 1. Specifically, we find very little evidence for visual RS in the occipital lobe, and these findings extend from pictures of faces to pictures of fruit confirming that these effects are not specific to faces. Moreover, we find that we continue to find robust responses in the occipital lobe to repeated face stimuli even when a single face is repeated at least 24 times (and as many as 64 times). This confirmed that the lack of visual RS in the occipital lobe is not arising from too few repetitions of an engaging or complex stimulus.

We also confirm and extend findings concerning the frontal lobe. Specifically, we continue to find a lack of RS in the frontal lobe to faces but find the same pattern to fruit stimuli. Moreover, we find that repeating the faces many more times (Super Repeated face condition) results in the largest response of the frontal lobe though differences between conditions are not significant. This confirms a lack of RS in the frontal lobe in response to visual stimuli and

suggests that if visual repetition modulates this region, it will be to produce repetition enhancement rather than suppression.

4. Experiment 3: expanding the frontal region of interest

In Experiment 2, we further delve into the findings concerning visual repetition suppression from Experiment 1. In Experiment 3, we focus on the findings that the frontal lobe exhibits strong repetition suppression for auditory but not visual stimuli. One limitation from the previous two experiments is that neural activity was only recorded from a very small portion of the frontal lobe. Moreover, while MR co-registration results consistently find that the two NIRS channels were localized in all babies to the frontal cortex, this region is immediately adjacent to the temporal lobe. In the current experiment, we employ a different configuration of the NIRS recording cap in order to record from the frontal lobe more broadly and determine whether the findings for the small portion of the left dorsolateral prefrontal cortex from Experiments 1 and 2 are consistent with other regions of the frontal lobe. To this end, we rotated the cap clockwise so that the panel previously recording from the occipital lobe is now recording from the temporal and left-lateral frontal lobe, and the panel previously recording from the temporal and left lateral frontal lobes is now recording broadly from the bilateral anterior frontal lobes.

We conduct another MR-coregistration with this new sample of infants and new cap configuration with the goal of defining 3 anatomical regions of interest. Two roughly correspond to the temporal and lateral frontal ROIs from the previous two experiments. The third ROI corresponds to the large bilateral medial frontal ROI and is the focus of the current experiment. With the exception of the changes in recording sites, the experimental paradigm was the same as Experiment 1. In other words, infants were exposed to words and faces in either repeated or variable presentation. Thus, the current experiment is a simple extension of the NIRS recordings of Experiment 1 with a new group of infants.

4.1. Methods

4.1.1. Participants

Twenty participants were included in the analysis of Experiment 3, aged 5–7 months old ($M = 6.1, SD = 0.46, Min = 5.34, Max = 6.8$ months); 9 female. The other participants heard a language other than English from their family no more than 15% of the time. Participants were identified as Caucasian only (85%, 17/20); African American (5%, 1/20), mixed race (5%, 1/20) or not reported (5%, 1/20). Three infants were identified as Hispanic; 1 did not have ethnicity reported and the rest were identified as non-hispanic. Five additional infants were excluded for the same criteria as the previous two experiments: 4 not looking long enough; 1 experimenter error.

4.1.2. Materials and design

This experiment was identical to Experiment 1 with the exception of the NIRS cap placement. In order to provide greater coverage of the frontal lobe, the cap was rotated clockwise so that the (formerly) rear and lateral panels of NIRS channels are (now) recording laterally and frontally. Specifically, the cap was placed so that most posterior row of the NIRS channels, in this new configuration, is placed directly over the left ear of the infant.

With the change in cap configuration, a new MR-coregistration analysis was conducted to define new anatomically-based ROIs (see Supplementary Materials for details on this analysis). Based on the MR-coregistration, we created 3 anatomical ROIs: One ROI, and the focus on this experiment, is an expanded **frontal ROI** which includes middle and superior frontal cortices. We will refer to this as the frontal ROI. This ROI has 5 channels selected based on a

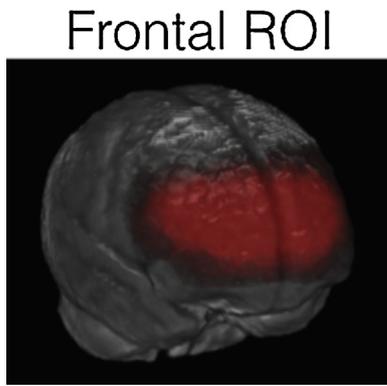


Fig. 10. Anatomically-defined bilateral frontal ROI for Experiment 3. This frontal ROI is an expansion of the frontal ROI recorded from in Experiments 1 and 2.

combination of channels which provide consistently good optical contact in the new cap configuration and the verified anatomical localization of these channels from the average MR template. Fig. 10 presents a visualization of the ROIs superimposed on an average infant MRI which weights the color-saturation based on the density of recordings over the sample of infants.

In addition, there were two ROIs roughly corresponding to the temporal and frontal ROIs reported in Experiments 1 and 2. However, the new cap configuration resulted in relatively poor recordings in these ROIs so these results are reported in the Supplementary Materials only for completeness (Fig. S6).

4.2. Results and discussion

Infants watched an average of 4.24 repetitions per condition (SD = 0.99) and a total of 17.0 blocks (SD = 3.95).

Average responses in the broad, bilateral frontal ROI (5 channels) exhibit the same pattern as found in Experiments 1 and 2 (Fig. 11). Specifically, there is evidence of repetition suppression in this region to auditory stimuli but not visual stimuli. Comparing responses to baseline, we find robust responses for the Variable Auditory ($t(19) = 3.11$, $p = 0.0058$) and the Repeated Visual ($t(10) = 2.32$, $p = 0.032$) but not Repeated Auditory nor Variable Visual ($t(19) < 1.4$, $p > 0.17$). Direct comparisons within stimulus modality revealed a significant reduction in response for Repeated Auditory stimuli compared to Variable Auditory ($t(19) = 2.60$, $p = 0.0089$) but no significant increase in response for the

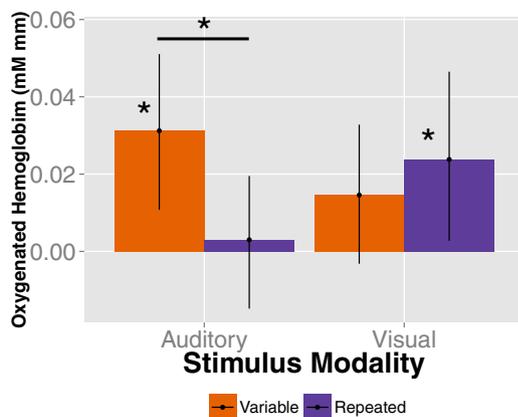


Fig. 11. Responses (averaged from 6 through 14.5 s) in the bilateral frontal ROI to auditory and visual stimuli in both variable and repeated conditions. Error bars indicate the standard error of the mean.

Repeated Visual ($p = 0.23$).² A repeated measures ANOVA revealed a significant interaction of stimulus modality and presentation type ($F(1,19) = 6.34$, $p = 0.021$) but no main effects. Together, these findings corroborate the previous two experiments that the frontal cortex exhibits repetition suppression exclusively for auditory stimuli. However, this new ROI extends this finding to broader regions in the frontal lobe.

5. General discussion

The current study is the first systematic investigation of the effects of stimulus repetition on the developing brain. Repetition suppression (RS) is one of the most established neural phenomena in cognitive neuroscience and is a well-characterized neural response to recent experience. Understanding repetition suppression in the developing brain is crucial for uncovering how the young brain adapts or changes in response to experience. Indeed, the phenomenon of RS exhibits a number of parallels with habituation, a behavioral phenomenon which is the foundation of numerous developmental studies with young infants (Turk-Browne et al., 2008). In addition, examining how the developing brain responds to experience can provide insight into the mechanisms underlying repetition suppression more broadly. While there are ongoing debates about the nature of the neural mechanisms underlying RS (e.g., is it adaptation or expectation? Krekelberg et al., 2006; Larsson and Smith, 2012; Summerfield et al., 2008), all accounts propose that the suppression of neural activity after stimulus repetition is a fundamental property of the perceptual cortex. If this is the case, infants should exhibit fundamentally the same neural responses to repetition as adults.

Since the modulation of perceptual cortices is considered the primary neural consequence of repetition, we propose that, if the infant brain is responding to repetition similarly to the adult brain, we would see repetition suppression (RS) in both occipital and temporal cortices in response to the repetition of visual and auditory stimuli, respectively. Surprisingly, this is not the pattern that we found. We found some evidence for auditory RS in the temporal cortex, but this pattern was weak and did not survive direct comparisons. More surprisingly, we did not find evidence of visual RS in the occipital lobe at all. Instead, we found consistently robust responses to the repeated visual stimuli in this region of the brain. This finding was replicated across two experiments and two sets of stimuli. Importantly, we increased the amount of visual repetition infants received and still observed a robust response (i.e., no RS) even after a single picture was presented 24–64 times. Thus, at best, we find weak evidence for auditory RS and no evidence for visual RS in infants.

Finding asymmetry in RS across perceptual modalities in the developing brain is novel but broadly consistent with previous work. While Nakano et al. (2009) and Dehaene-Lambertz et al. (2006) both report effects of repetition in the temporal lobe of young infants, there have been no demonstrations of visual RS in the occipital lobe early in development. In fact, a close look at the literature reveals a number of convergent findings that visual RS might be late to develop. Notably, Scherf et al. (2011) employed fMRI to examine RS for faces and houses in children, adolescents and adults. They reported a broad pattern of visual RS in adults but no evidence of visual RS in children. Their findings do not have the limitations of fNIRS, most notably the limited depth of recording below the cortical surface and poorer spatial resolution.

² We conducted a one-tailed t -test looking for an increase in response to repeated stimuli compared to variable based on the results from the two previous experiments.

Kobayashi and colleagues examined the effects of repetition of faces using fNIRS with young infants (Kobayashi et al., 2011, 2014) with broadly consistent findings as they report RS for faces but only starting at 7 months of age. However, these results must be interpreted with caution as the studies are consistently under powered (i.e., only 12 infants per sample with a very high attrition rate) and report statistics without correcting for multiple comparisons. They also engaged in 'double-dipping' by conducting ANOVAs on channels found to exhibit response profiles consistent with their hypotheses. In addition, the authors recorded only from the temporal cortex in an effort to reveal identity-specific responses in the infant brain as a face is presented in varying views and expressions (e.g., neutral, smiling, puffing cheeks) making it difficult to compare with current findings as we consider responses in the occipital lobe as the repetition of identical faces (consistent with numerous adult studies, de Gardelle et al., 2013; Gilaie-Dotan and Malach, 2007; Rotshtein et al., 2005; Scherf et al., 2011). However, we do also examine responses in the temporal ROI to visual repetition and also find no evidence for visual RS (Fig. S3). This comparison too is difficult to make as Kobayashi and colleagues record more posterior regions of the temporal lobe than the current study and this is the site of their findings. Overall, the inconsistent findings between Kobayashi and colleagues previous work and the current study speak to differences in the motivation for employing faces in a repetition suppression design. The goal of the current work is to examine visual repetition suppression in the many low- and mid-level visual regions and faces were employed to maintain infant attention while simultaneously varying these low- and mid-level features. Kobayashi and colleagues were focused on higher-level visual processing of faces and are employing repetition suppression as a method for uncovering developmental changes and locations of face processing in the infant brain. These differences in goals for these papers must be kept in mind when evaluating the differences in methods including specific stimuli, baselines, and probe locations.

While the current discussion largely restricts itself to neuroimaging methods that can make spatial inferences, ERP studies of RS have found similar results: while there is evidence of auditory RS involving both temporal and frontal cortices (Dehaene-Lambertz and Dehaene, 1994), ERP studies of visual RS have also largely reported a lack of visual RS in the developing brain (see Nordt et al., 2016, for a recent review). To be clear, some fNIRS studies have employed visual stimuli and found clear evidence for RS. However, in these cases low-level visual repetition was controlled in order to examine effects of repetition in domains of higher-cognition such as number (Hyde et al., 2011) or goals (Southgate et al., 2014). Thus, our current finding of a lack of visual RS is not without precedent in the literature while, in contrast, there are clear demonstrations with auditory RS in the infant brain.

As reviewed in Nordt et al. (2016), a lack of evidence for visual RS, especially in children, is surprising and in clear contrast to behavioral studies which have established that children readily discriminate between exemplars of faces. There are numerous (not mutually exclusive) possibilities to account for this which are important areas of future research. First, these findings suggest that RS is not the basis of recognition itself, but perhaps the outcome of this recognition process. Second, it could be that requiring infants to direct their gaze consistently to a diversity of visual exemplars could dilute RS to visual stimuli. Because auditory stimuli can be attended to without sustained visual attention, the superior RS to auditory stimuli could be the result of easier access. Third, it could be that early in development, individuals do not exhibit RS unless there is a functional reason to do so. This account would predict that including a task where behavior is benefitted from detecting or anticipating repeats would result in RS. If this were the case, it would support a view of RS as being driven by expectations and/or

top-down signals rather than lower-level neural adaptation, and differences in engagement of higher-level cortices when stimuli are repeated would lead to differences in RS in perceptual cortices. This last possibility receives some support from the pattern of frontal lobe involvement that we see in this task. However, it is not immediately clear why there would be differences in the tendency to form expectations in the auditory modality compared to the visual modality and is an important area for future research.

While we do not find evidence for RS in either perceptual cortex and not even a suggestion of visual RS in the occipital lobe, we find strong evidence for RS in the infant frontal lobe but only for auditory stimuli. We confirm this pattern across 3 experiments: We find significant attenuation of neural activity to repeated compared to variable auditory stimuli in the infant frontal lobe but find no evidence of attenuation of responses for visual stimuli. In fact, if visual repetition has any effect on the frontal lobe, it trends toward repetition enhancement. Thus, we find differential engagement of the infant frontal lobe to auditory and visual stimuli and only strong evidence for auditory RS.

Studies implicating frontal lobe involvement in RS suggest an important, functional connection between frontal lobe and perceptual system modulations in response to repetition. The locations of frontal lobe RS are similar to those reported in the current study (Ghuman et al., 2008, e.g., left inferior frontal gyrus for auditory stimuli). Interestingly, numerous studies have found evidence of visual RS in the adult brain but always in combination with RS in the relevant perceptual cortices (e.g., Eriksson et al., 2008; Race et al., 2009; Zago et al., 2005). Ghuman et al. (2008) found that visual stimulus repetition both decreased activity in perceptual and frontal cortices but also *increased* neural synchrony between these regions. Moreover, the amount of neural synchrony correlates with behavioral facilitation resulting from repetition. There is more indirect evidence that the adult frontal lobe is modulated by repetition from the mismatch negativity (MMN) literature. Specifically, the frontal cortex has been implicated in auditory change detection (i.e., increases in activity with auditory novelty). Again, these frontal lobe findings are found in concert with activity changes in perceptual cortices (e.g., Schönwiesner et al., 2007). Thus, numerous studies have found frontal lobe modulation as a result of repetition (or novelty) and, notably, these frontal lobe findings are always paralleled with modulation of the relevant perceptual cortices.

While there are numerous accounts of the frontal cortex's involvement in RS, all accounts suggest a functional, modulatory role of this region of the brain in concert with perceptual cortices. While some of these accounts are feed-forward in nature (e.g., the frontal lobe is involved in the allocation of attention after a sufficient change is detected Schönwiesner et al., 2007), the majority of these accounts implicate the frontal lobe in feedback, top-down modulation of more posterior cortices. Schacter et al. (2007) propose that repetition results in both perceptual-tuning but also "a second mechanism that primarily reflects changes in the prefrontal cortex that drive behavioral priming effects in a top-down manner" (p. 174). Importantly, some researchers have argued that the increased efficacy of top-down signals from the frontal lobe drive reductions in perceptual cortex activity with increased repetition (Race et al., 2009). This account is similar to the arguments that expectation is necessary for perceptual cortex RS even though the frontal lobe is not directly implicated in these arguments (Summerfield et al., 2008).

Current results also point to an important connection between frontal lobe modulation from repetition and perceptual cortex RS: We report that the developing frontal lobe is modulated only with types of repetition that also modulate the relevant perceptual cortices. While largely speculative, the current findings suggest that the frontal cortex is involved in top-down modulation of the

perceptual cortices when stimuli are repeated. The most direct evidence is that there is a strong pattern of RS in the frontal lobe but only indirect evidence for RS in the relevant perceptual cortex suggesting a more primary role for the frontal lobe compared to the perceptual cortices. Moreover, the asymmetry in RS across stimulus modalities could be arising from the asymmetry in connectivity between the frontal lobes and the relevant perceptual cortices. Investigations into white-matter tracts in the young brain suggest that there is an early developing connection between the temporal and frontal lobes that can support communication between these cortical regions during auditory processing (Dubois et al., 2009). Studies of functional connectivity in young infants also suggest that there is early connectivity between temporal and frontal cortices (Gao et al., 2011; Homae et al., 2010). Importantly, even more compelling than the clear absence of connectivity between the frontal and occipital regions early in life, Homae et al. (2010) report significant decreases in connectivity between the frontal and occipital regions of the brain from birth to 6 months. Thus, there is differential connectivity between perceptual cortices supporting visual and auditory perception (occipital and temporal cortices respectively) and the frontal lobe, and this asymmetry mirrors that asymmetry that we observe in RS in these perceptual systems. In combination with studies in adults pointing to a role of the frontal lobe in generating top-down signals to modulate perceptual cortices in response to repetition, this work suggests that a similar functional role is being played by the frontal lobe early in development. Of course, an alternative possibility which cannot be conclusively ruled out is that perceptual cortex modulation is a necessary pre-cursor to frontal cortex modulation with stimulus repetition, or that sub-cortical systems are crucial to RS but are not assessed with fNIRS. These various accounts have different developmental predictions which are important avenues for future research.

Overall, the current paper provides the first evidence that the developing brain does not respond to repetition in the same way that the mature brain does both in terms of the strong modulation of activity in the frontal lobe over perceptual cortices as well as the differential modulation for auditory and visual stimuli. Moreover, we provide some initial evidence that the frontal lobe might be involved in the development of RS in perceptual cortices. Specifically, strong modulation of the frontal lobe to stimulus repetition might support RS in perceptual cortices through top-down modulation.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.dcn.2016.11.002>.

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