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# Neural processing of auditory temporal modulations in awake infants

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28 **Abstract**

29

30 The Amplitude Modulation Following Response is the steady-state auditory response signaling  
31 phase-locking to slow variations in the amplitude (AM) of auditory stimuli, that provide fundamental  
32 acoustic information. On a developmental perspective, the AMFR has been recorded in sleeping  
33 infants, compared to sleeping or awake adults. The lack of AMFR recordings in awake infants limits  
34 conclusions on the development of phase-locking to AM. Moreover, previous studies assessing phase-  
35 locking to AM using non-speech carriers have not included slow AM rates (<20 Hz), which are  
36 particularly important for speech processing. This study aimed at disentangling these issues by  
37 recording the AMFR with electroencephalography: in awake infants (3- and 10-month-olds) and  
38 awake young adults; for both slow and faster modulation rates (8 Hz and 40 Hz). The AMFR was  
39 observable at 8 Hz at all ages (40%, 60%, 33% of significant AMFR at 3 months, 10 months and  
40 adults, respectively), but only adults showed reliable responses at 40 Hz (6% of significant AMFR at  
41 both 3 and 10 months, 100% in adults), thus ruling out the possibility that sleep has a suppressing  
42 effect on the response. This pattern might be explained by developmental differences in the sources  
43 of neural processing of faster AM rates.

44

## 45 I. INTRODUCTION

46 Auditory processing is thought to result from the action of a series of filters extracting spectral  
47 information from high to low frequencies within the peripheral auditory system, the cochlea (Moore,  
48 2004). At the output of cochlear filters, sounds are then modeled as a series of narrowband signals  
49 modulated in amplitude over time. In each narrowband signal, changes in amplitude can be further  
50 decomposed. Specifically, two important time scales have been identified: a relatively fast one,  
51 corresponding to frequency modulation (FM) cues, and a relatively slow one, amplitude modulation  
52 (AM) cues-(Drullman, 1995; Shannon et al., 1995).

53 AM processing can be modeled as the operation of a central bank of modulation filters (Dau et  
54 al., 1997) organized in neural sites that are thought to be selectively tuned to specific AM rates (Giraud  
55 et al., 2000; Joris et al., 2004; Kim et al., 2020; Liégeois-Chauvel et al., 2004).

56 The processing of AM information is fundamental in auditory perception (e.g., Joris et al., 2004),  
57 crucial for speech perception (Drullmann, 1995; Shannon et al., 1995) and for the mechanics of  
58 cochlear implants. However, the early development of AM processing in humans is not yet fully  
59 characterized.

60 Behavioral studies have shown that young listeners always exhibit worse AM sensitivity when  
61 compared to adults (Hall and Grose, 1994; Walker et al., 2019). However, other studies also showed  
62 similar effects, in infants and adults, of AM rate on AM detection thresholds. Specifically, when  
63 measuring 10-Hz AM detection thresholds, 3-month-old infants have been shown to require about  
64 10 dB more of AM depth than adults (Walker et al., 2019) when tested with a narrow-band noise  
65 carrier. This notwithstanding, the cut-off frequency of the Temporal Modulation Transfer function  
66 (TMTF, the empirical function relating AM detection to the modulation frequency of the stimulus),  
67 was not different between infants and adults, showing analogous temporal resolution (i.e., the limit in  
68 the auditory system's ability to follow AM fluctuations as these become faster). The finding of adult-  
69 like temporal resolution despite worse AM detection in very young listeners supports the hypothesis  
70 that developmental differences in AM detection may not preponderantly relate to the maturation of

71 sensory coding for AM cues (which seems to be early attained), but rather to ‘processing inefficiencies’,  
72 i.e., lesser efficiency in the use of successfully extracted AM information in younger listeners (Cabrera  
73 et al., 2019; Dau et al., 1997).

74 Electroencephalography (EEG) offers the opportunity to look into these processing differences  
75 at the neural level. In particular, EEG can measure the auditory brain activity following the modulation  
76 rate of sinusoidally amplitude modulated tones (Picton et al., 2003). This response, the so-called  
77 Amplitude-Modulation Following Response (AMFR), or Envelope-Following Response (EFR), is  
78 phase-locked to the amplitude envelope of auditory stimuli. As such, it describes the auditory response  
79 that encodes the periodicity of the temporal envelope.

80 The AMFR was measured in 1-month-old infants and adults in a series of pioneering studies (Levi  
81 et al., 1993, 1995). In particular, it was recorded for modulations ranging between 20 and 80 Hz, in  
82 sleeping infants as compared to awake adults. The largest response (i.e., the stronger AMFR relative  
83 to background neural noise) detected in sleeping infants and sleeping adults corresponded to  
84 modulations of 80 Hz; conversely, the largest responses detected in awake adults corresponded to  
85 modulations of 40 Hz. Thus, sleep, either natural or chemically induced, has a significant effect on the  
86 AMFR in adults (Levi et al., 1993, Picton et al., 2003).

87 A second study presented sleeping 1-month-old infants AM tones with carrier frequencies of 500,  
88 1000, or 2000 Hz modulated at 80 Hz and the same tones modulated at 40 and 80 Hz to adults (Levi  
89 et al., 1995). The results showed no difference between infants and adults for 500 and 1000 Hz carrier  
90 frequencies. However, infant’s AMFRs relative to background neural noise was smaller than adults’  
91 for the highest carrier frequency (2000 Hz). This suggests that, although robust phase locking to the  
92 sound envelope is observed by 1 month of age, age-related differences in the AMFR can be detected,  
93 depending on the carrier frequency.

94 Finally, a study comparing the AMFR evoked by AM-white noise (i.e., a broadband noise sinusoidally  
95 modulated in amplitude) obtained in naturally sleeping newborns versus sedated 2-year-olds showed  
96 developmental changes in response morphology and improvements in AMFR detectability against

97 background noise between the rates of 20-200 Hz (Nodarse et al., 2012). In fact, a 40Hz-AMFR was  
98 not reliably observed until 2 years of age in some studies, with its magnitude increasing with age  
99 (Nodarse et al., 2012; Pethe et al., 2004).

100 Crucially, in all EEG experiments mentioned above, infants were asleep. This was done to ensure  
101 cooperation during long experiments. However, knowing that sleep influences AMFR responses in  
102 adults (Levi et al., 1993), it is necessary to test the AMFR in awake infants, thus allowing a more  
103 reliable comparison of the responses observed at different ages. Furthermore, only AMFRs for high  
104 rates of modulations ( $> 20$  Hz) have been recorded in infants, so far, in spite of the fact that slower  
105 AM rates are known to be particularly important for speech perception (Shannon et al., 1995). Cortical  
106 tracking to slower AM rates in infancy have been reported by studies assessing phase-locking to AM  
107 of the speech signal (ex., Ortiz Barrajas et al., 2021; Attaheri et al., 2022), which provided important  
108 evidence that infants track the envelope of continuous speech at different time scales (at least, at the  
109 level of sentence prosody  $\sim 2$  Hz, and at the syllabic level  $\sim 4$  Hz). These investigations, in particular,  
110 contributed clarifying the abilities of the infant's brain to track speech temporal cues. However, it is  
111 important to note that the underlying auditory mechanisms of this ability are not yet fully understood  
112 yet. Exploring the AMFR with non-speech sounds, on the other hand, allows to assess AM tracking  
113 for highly controlled acoustic stimuli. In fact, using pure tones as an AM-carrier entails only AM  
114 fluctuations specific to a given rate and stimulates only a given region on the basilar membrane. This  
115 allows to draw specific conclusions on the development of the auditory mechanisms involved in  
116 general AM tracking, whereas studies conducted with speech stimuli cannot, as speech carriers are  
117 more complex in their spectrum and contain temporal fluctuations at different rates (i.e., AM and FM)

118 To sum up, the aim of the present study was twofold: 1) to compare AMFRs in infants and in  
119 adults while using the same experimental conditions (all participants awake), and 2) to compare the  
120 AMFR obtained with slow versus faster modulation rates. Specifically, we measured AMFR in awake  
121 infants and adults at two modulation rates: 8 vs 40 Hz, using a pure tone carrier of 1000 Hz, carrier  
122 frequency which, based on the literature, should elicit a response in both infants and adults (Levi et

123 al., 1993; Savio et al., 2001). The (slow) modulation frequency of 8 Hz was selected because previous  
124 literature has shown strong links between this frequency range and speech perception. Indeed, strong  
125 degradation of performance in speech perception in quiet has been shown when speech stimuli are  
126 vocoded by filtering modulation frequencies including and above 8-10 Hz (Drullman, 1995).  
127 Moreover, evidence has been put forward of a relationship between AM detection thresholds as  
128 measured using non-speech stimuli modulated at 8 Hz and speech in noise perception abilities  
129 (Cabrera et al., 2019).

130 The present experiments focused on infants of 3 months because this is the earliest age at which  
131 infants have been shown (behaviorally) to have similar TMTF to those of adults (Walker et al., 2019),  
132 suggesting adult-like temporal resolution and AM processing. Additionally, we also recruited a group  
133 of 10-month-old infants, with the goal to investigate the maturation of the AMFR during the first year  
134 of life and, particularly, in a period of intense linguistic development (Werker et al., 1984). Indeed,  
135 between 3 and 10 months of life, infants undergo a process of perceptual reorganization resulting in  
136 the fact that they become, as adults, better able to process the speech sounds that belong to their  
137 native language(-s), while at the same time decreasing precision in processing speech sounds that do  
138 not belong to their native language. This process is crucial for linguistic development (Kuhl, 2004)  
139 and is underpinned by reorganization in the neurofunctional treatment of native versus non-native  
140 speech sounds (Minagawa-Kawai et al., 2007). Thus, observing the characteristics of the AMFR to a  
141 target frequency relatively to background noise (i.e., signal-to-noise ratio, SNR) in awake 10-month-  
142 olds can also shed light on the effectiveness of the AM processing skills that are available to human  
143 infants during such crucial tuning to the speech signal.

144 In a first experiment, three groups of participants (one group of 3-month-old infants, one group  
145 of 10-month-old infants, and one group of adults) were presented with AM tones played at 65 dB SPL  
146 (sound-pressure level) in free field. All participants were awake. In a second experiment, we  
147 manipulated the intensity level of stimulus presentation. Specifically, intensity was increased up to 75  
148 dB SPL for a new group of 3-month-old awake infants to assess whether intensity levels could

149 influence the neural response to the target AM rates (Cone & Garinis, 2009). Apart from the intensity  
150 difference, the recording procedure was the same as in the first experiment. Our hypotheses were as  
151 follows. If the infant auditory system is sensitive to both slow and fast AM fluctuations from early on,  
152 we should observe similar AMFR-SNR in the three age groups (3-month-olds, 10-month-olds and  
153 adults), at both 8 and 40 Hz modulations. Inversely, if temporal auditory processing takes a long time  
154 to develop, we should observe an effect of age on the strength of AMFR (characterized by a higher  
155 SNR) at both rates. Specifically, if differences are observed between slower versus faster AM rates,  
156 this could relate to the development of sensory processing coding for temporal information. In other  
157 words, if smaller AMFR-SNR for faster AM rates are only observed in infants as compared to adults,  
158 this might be due to limited temporal resolution; but if smaller AMFR-SNR are observed in infants  
159 irrespectively of AM rate, this could rather relate to the development of higher stages of auditory  
160 temporal processing (e.g., changes in the neural transmission of temporal information along the  
161 auditory pathway enhancing processing efficiency with age).

162

163        **II.     EXPERIMENT 1**

164        **A. Methods**

165            **1. Participants**

166            Three different age groups of 15 participants each took part in the present study: 3-month-  
167 old infants (aged between 2 months 16 days and 3 months 22 days, mean age = 3 months, sd = 12  
168 days; 9 female); 10-month-old infants (aged between 9 months 11 days and 10 months 5 days, mean  
169 age = 9 months 22 days, sd = 8 days, 7 females); young adults (aged between 20 and 30 years; mean  
170 age = 23.2 years, sd = 2.8 years; 14 females). Group size was decided according to previous studies  
171 recording the AMFR in young infants (e.g. Cone & Garnis, 2009, Levi et al., 1993, Nodarse et al.,  
172 2012). Informed consent forms were obtained from all infants' legal guardians and adult participants.

173            All participants were raised in monolingual French families (exposed less than 10% of the time  
174 to an additional language than French). All infants were born full term (> 37 gestational weeks), with  
175 a birth weight over 2.5 kg, had no history of otitis media at testing, no risk factors for hearing loss nor  
176 language disorder, and had no history of health or developmental concerns. They also all passed the  
177 newborn-hearing screening. For adult participants, absolute auditory thresholds were assessed with  
178 pure tones for both ears at octave frequencies between 0.25 and 8 kHz prior to testing. The mean  
179 pure-tone average threshold was considered as normal if equal or below 20 dB Hearing Level.

180            Data from an additional two 3-month-olds were excluded because recordings were still too  
181 noisy after processing. Data from an additional six 10-month-olds were excluded because recordings  
182 were too noisy (N=4), the infant was too fussy to complete the task (N=1) and parents interfered  
183 during recording (N=1). Those data were excluded from the analyses.

184



185            **2. Stimuli & Procedure**

186            Two 100% sinusoidally amplitude modulated pure tones centered at 1027 Hz were used as  
187 stimulus (John et al., 2004; Levi et al., 1993). The AM rate was set either to 8 or to 40 Hz (as shown  
188 in **Figure 1.A**). Each sound was 4 min-long including 50-ms raised-cosine onset/offset ramps, and  
189 presented continuously through 2 loudspeakers (Bose ® Companion 20) positioned at 0-degree  
190 Azimuth on each side of a computer screen. Participants sat in front of the screen at a distance of ~  
191 1 meter. Infants were sat onto one of their parents' laps. In experiment 1, the intensity level was  
192 calibrated at 65 dB SPL at the place where participants were positioned.

193            Each participant was exposed to two 4-min long blocks of sounds, one for each modulation  
194 rate (8 and 40 Hz modulations), presented in a counterbalanced order between participants. After the  
195 first auditory stimulation, a short break was proposed and the second stimulation started soon after.

196            Participants watched a silent animated cartoon during the whole experiment. Infants were  
197 provided with toys and distraction when they were not interested in the cartoon in order to reduce  
198 movement.

199            All methods were carried out in accordance with relevant guidelines and regulations, Informed  
200 consent forms were obtained from all infants' legal guardians and adult participants as approved by  
201 the university ethic committee (CER-U Paris).

202

203            **3. EEG setup, signal processing and analyses**

204            The EEG system used for the recording was Brain Vision (version v1.0.9). Three active central  
205 electrodes (Fz, Cz, Pz from 10-20 system, the ground positioned at Fpz) were used, based on previous  
206 studies (John et al., 2004; Levi et al., 1993; Nodarse et al., 2012) were positioned on a cap with the  
207 ground and 2 external electrodes were positioned at mastoids (acting as online references) as  
208 represented in **Figure 1.B**. The sampling rate during recording was set to 10 kHz. The cap size was  
209 determined prior the experiment following each participant head size.

210 Signal processing was done in Matlab (version 2021b) using EEG lab (version 2021.0). For  
211 each electrode recording, the continuous EEG signal was first divided into 2 epochs: one containing  
212 the recording for the 8 Hz stimulation and one for the 40 Hz one. Then the signal was band-pass  
213 filtered from 6 to 46 Hz (using the FIR from EEGLAB). In each condition, a Fast Fourier Transform  
214 was used to calculate the complex frequency spectrum of each epoch, resulting in a frequency  
215 resolution of 0.0024 Hz.

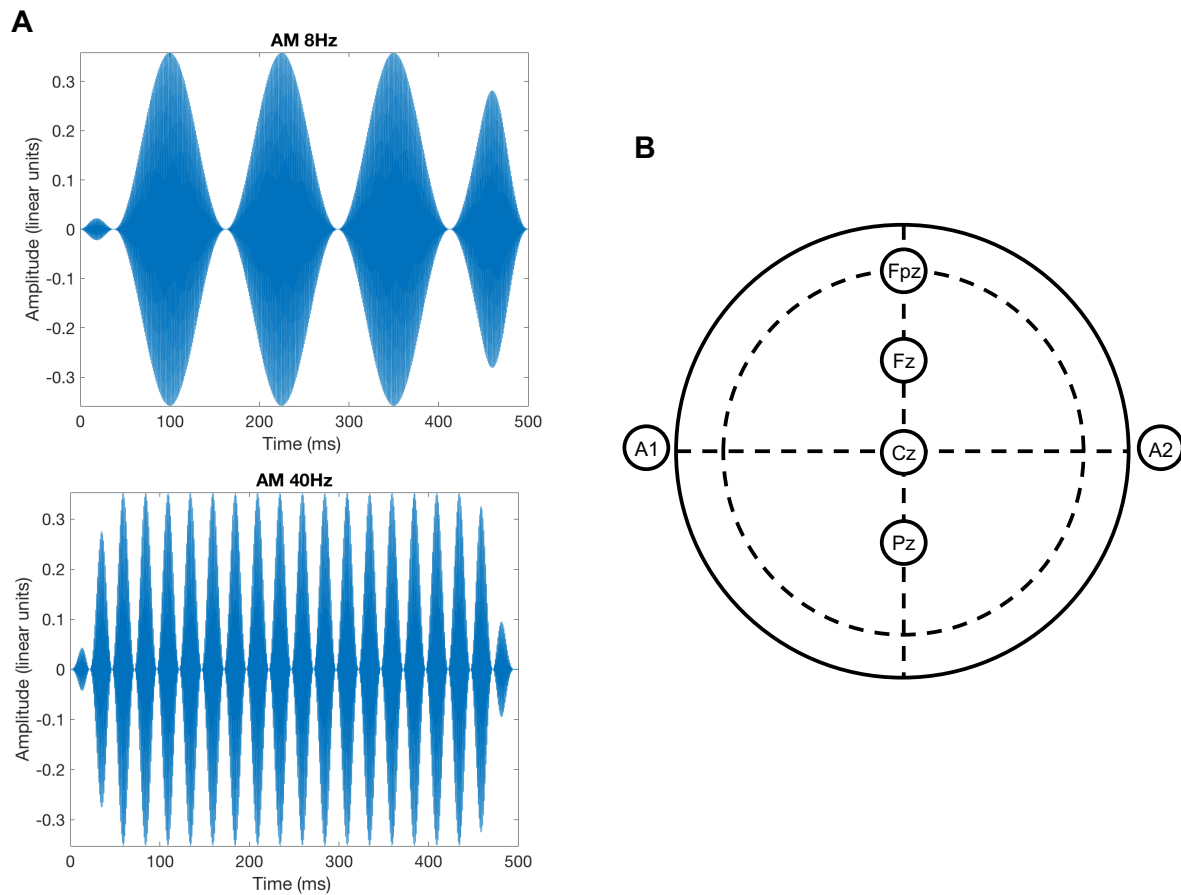
216 For each participant, the maximum amplitude value of the EEG signal was measured between  
217 7.8 and 8.2 Hz and between 39.8 and 40.2 Hz for the 8 and 40 Hz conditions, respectively. The noise  
218 floor was computed as the mean of squares at either side of the modulation frequency ( $\pm 3$  Hz) not  
219 including portions of the target signal window itself (Cone and Garinis, 2009; Mepani et al., 2021;  
220 Vanvooren et al., 2015). The signal-to-noise ratio (SNR) was then defined as the ratio between the  
221 maximum amplitude at the target frequency and the noise floor. Note that we will not compare directly  
222 SNR values between the 8 and 40 Hz conditions as the EEG noise is significantly higher at lower  
223 frequencies (Cellier et al., 2021).

224 A visual inspection of the responses recorded in each condition revealed that the best  
225 responses (i.e., overall less noise) were observed at Fz electrodes for infants. Moreover, comparison  
226 of the SNR values between electrodes and combination of electrodes confirmed that the SNR was the  
227 highest at Fz for infants. Thus, the following analyses focused on comparing the responses at Fz  
228 between age groups.

229 In the analyses, the individual responses at each modulation rate were considered to be statis-  
230 tically significant using a F-ratio estimating the probability that the amplitude at the target frequency  
231 is significantly above the neighboring frequencies (noise calculated over  $> 120$  points at each side of  
232 the signal frequency) at a level of  $p < .05$ . More precisely, the SNR of the AMFR was compared to  
233 the critical value of 2.9957 corresponding to a F value for  $\alpha = 0.05$  with 2 and  $>120$  degrees of freedom  
234 (John et al., 2004; Valdes et al., 1997). Then, age group comparisons were done. The AMFR-SNR in  
235 dB were normally distributed (Shapiro-Wilk test,  $p > .05$  for all conditions/groups), but, as each group

236 amounted to 15 participants only, non-parametric tests (Kruskal-Wallis test for k independent samples  
237 and Mann-Whitney U for 2 independent samples) were used to evaluate the effect of Age group on  
238 the SNR data at 8 and 40 Hz independently.

239



240

241 **Figure 1. A.** Waveforms of two pure tones representing the variations in amplitude over time of a  
242 tone modulated at 8 Hz (upper panel) and at 40 Hz (lower panel). A 50-ms on and off ramp was  
243 applied. **B.** Schematic representation of the EEG setup including: the 3 central electrodes used for  
244 AMFR measurement (Fz, Cz and Pz); the ground, as placed at Fpz; the 2-linked mastoids (A1, A2),  
245 used as online reference.

246

247 **B. Results**

248 The grand averages of the AMFR for the 8 Hz and 40 Hz conditions are shown in **Figure 2**  
249 for each group. As shown in the literature (Cellier et al., 2021), the level of noise was higher in the 8  
250 Hz condition than in the 40 Hz condition for all groups as revealed by non-parametric Wilcoxon test  
251 for paired samples ( $Z = -3.412, p = .001$ ;  $Z = -3.416, p = .001$ ;  $Z = -3.420, p = .001$ ; for 3-month-olds,  
252 10-month-olds and adults, respectively). Moreover, infants showed significantly higher levels of noise  
253 than adults as shown by U test of Mann-Whitney ( $U = 551.500, n \text{ adults} = 32, n \text{ infants} = 58, p =$   
254  $.001$ ). Note that, even though more noise was observed in infants than adults, this difference was  
255 taken into account by the SNR calculated for each participant (the ratio between the maximum  
256 amplitude at the target frequency and the noise floor). All three groups displayed a peak at 8 Hz in the  
257 average response, but only the group of adults showed a peak at 40 Hz.

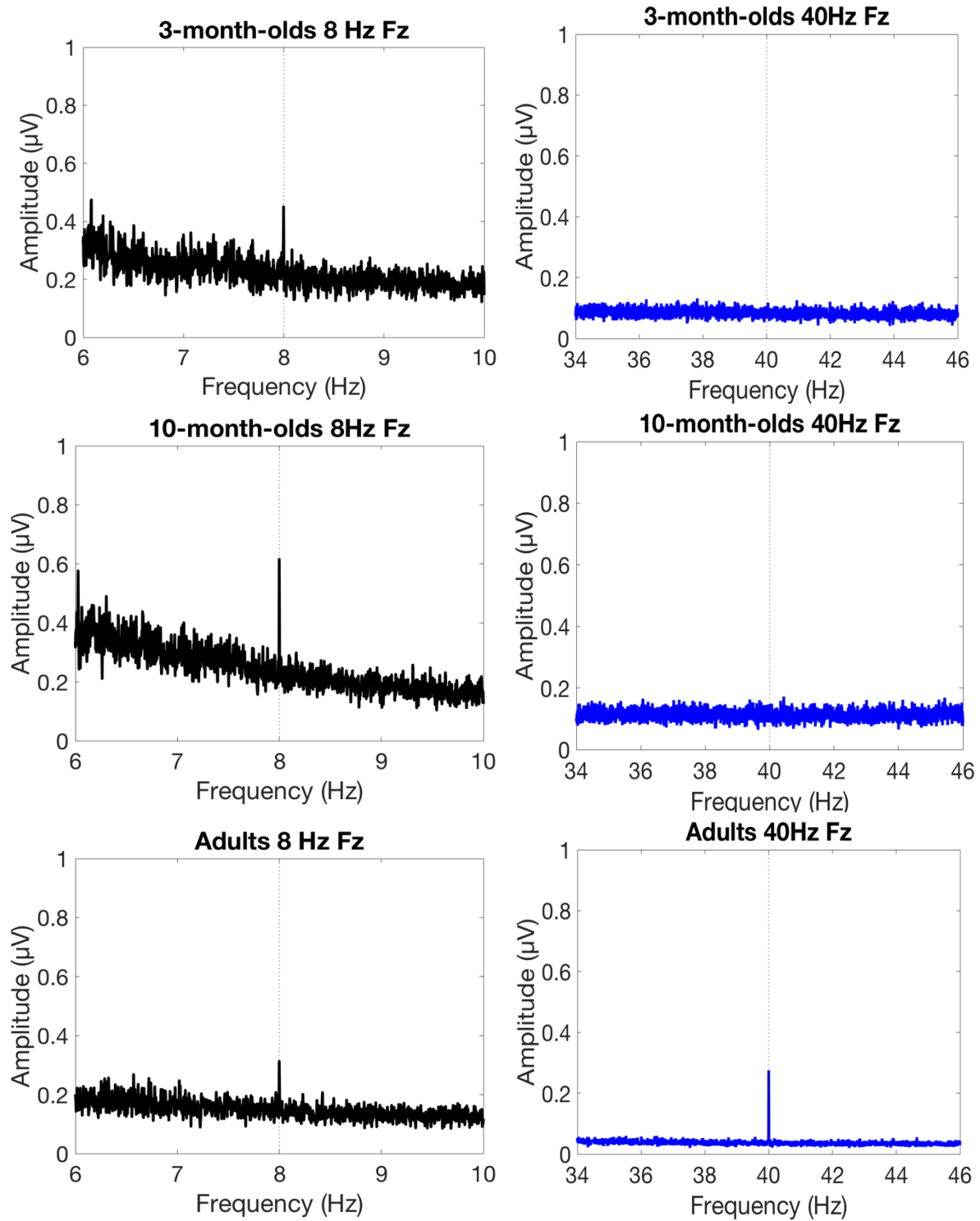
258 Individual SNR of the AMFR in each group is represented in **Figure 3**. The percentage of  
259 significant AMFR (representing the proportion of participants whose AMFR was above chance level)  
260 at 8 Hz was 40%, 60% and 33% for 3-months, 10-months and adults, respectively. At 40 Hz, a  
261 different pattern was observed, as significant AMFR were observed only in 6% of the 3-month-olds  
262 and 6% of the 10-month-olds, but in 100% of the adult group.

263 The Kruskal-Wallis test for independent samples showed no effect of Age group on the  
264 AMFR-SNR values in the 8 Hz condition [ $H(2, n = 45) = 1.573; p = .455$ ]. However, a significant  
265 effect of Age group was observed in the 40 Hz condition [ $H(2, n = 45) = 29.799; p < .001$ ]. To further  
266 assess this main effect of Age, comparisons 2 by 2 were run using the U test of Mann-Whitney (i.e.,  
267 3-month-olds vs adults; 10-month-olds vs adults; 3-month-olds vs 10-month-olds). These  
268 comparisons confirmed that the AMFR-SNR values were significantly higher in the 40 Hz condition  
269 for adults than for 3-month-olds ( $U=1.000, p < .001$ ) and for adults than for 10-month-olds ( $U=0, p$   
270  $< .001$ ), but did not differ between 3- and 10-month-olds ( $U=85.000, p = .233$ )<sup>i</sup>.

271 In order to assess whether the absence of AMFR at 40 Hz in infants may be related to the  
272 intensity level of presentation (Cone and Garinis, 2009), we tested a second group of 3-month-old

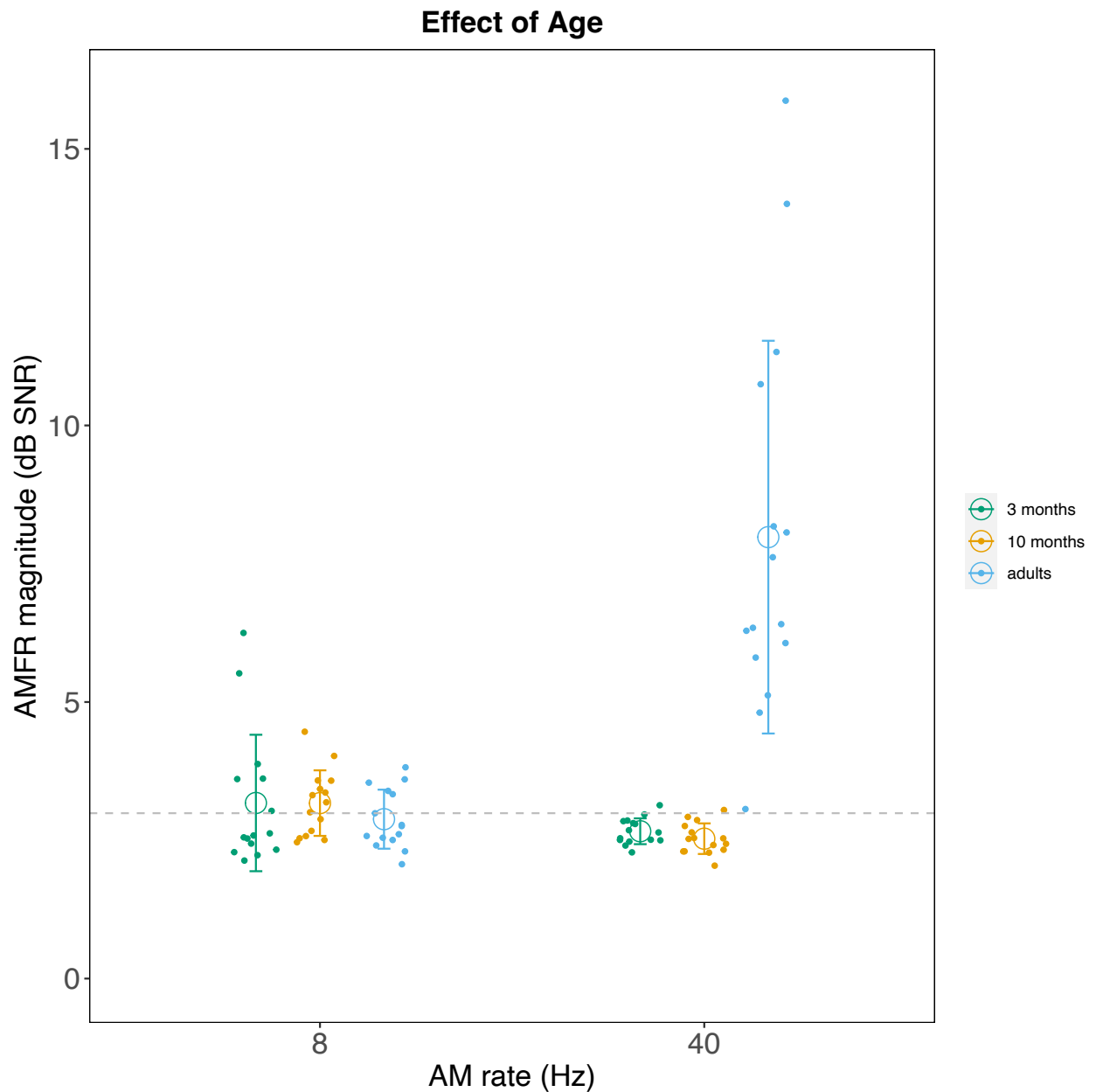
273 infants in the exact same conditions, but the sound level was set to 75 dB SPL. Ten-month-old  
274 participants were not included in this second experiment because, as temporal resolution for AM  
275 information is mature by 3 months of life (Walker et al., 2019), if an increase in the AMFR at 40 Hz  
276 was detectable due to increased intensity in stimuli presentation, it should be observed starting from  
277 this early age. As adult listeners already showed a strong AMFR at 40 Hz when stimulated at 65 dB  
278 SPL, we did not include a new group of adults in this second experiment.

279



281

282 **Figure 2.** Grand average (N=15) of the AMFR (in  $\mu\text{V}$ ) for the 8 Hz (left panels) and 40 Hz (right  
 283 panels) conditions in the three age groups (3-month-olds, 10-month-olds and adults from the top  
 284 panel to the bottom panel, respectively). The data are shown for the Fz channel.



285

286 **Figure 3.** Individual AMFR magnitudes (in dB SNR) are represented in each group (closed circles in

287 green, orange and blue for 3-, 10-month-olds and adults, respectively). Open circles represent the

288 group averages in the 8 Hz and in the 40 Hz condition. The error bars represent the standard deviation.

289 Higher magnitude corresponds to higher AMFR peaks. The horizontal grey dashed line represents the

290 critical value for 0.05 level of significance for the F ratio.

291

### 292 III. EXPERIMENT 2

#### 293 A. Methods

##### 294 1. *Participants*

295 A second group of 15 3-month-old infants participated in the second control experiment (aged  
296 between 2 months 16 days and 3 months 22 days, mean age = 3 months, sd = 12 days, 9 girls). The  
297 inclusion/exclusion criteria were the same as in Experiment 1. One additional infant was not included  
298 in the final sample because s/he was too tired to complete the task.

299

##### 300 2. *Stimuli, Procedure, EEG setup, signal processing and analyses*

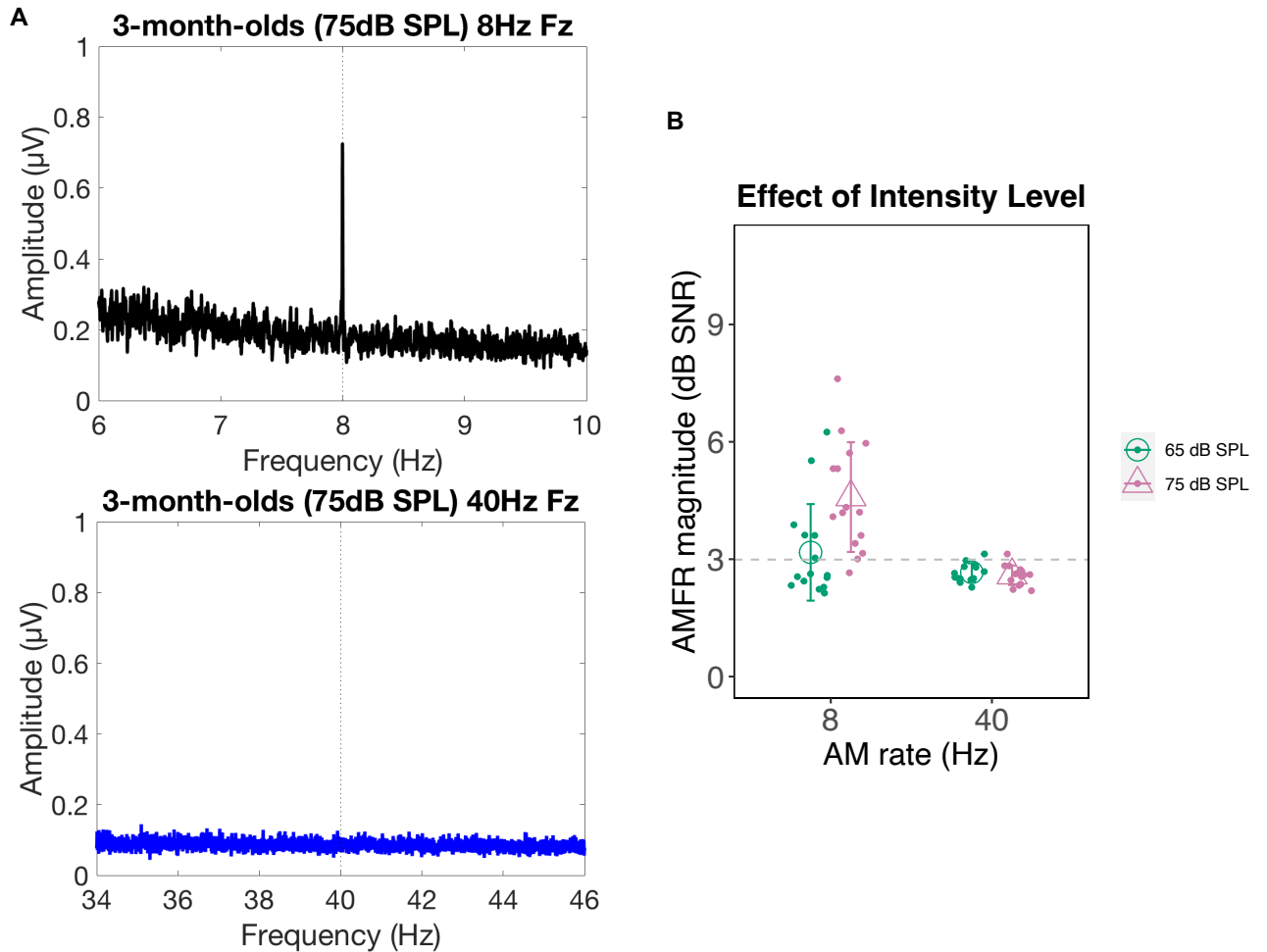
301 Similar stimuli and procedure from Experiment 1 were used except that the presentation level  
302 was set at 75 dB SPL. Analogous EEG setup, signal processing and analyses were used.

303

#### 304 B. Results

305 The grand average of the AMFR for the second group of 3-month-olds tested at 75 dB SPL  
306 is represented at each rate in **Figure 4.A**. At 8 Hz, significant AMFRs were observed in 93% of the  
307 3-months stimulated at 75 dB SPL, but only 6% showed a significant AMFR at 40 Hz. The individual  
308 SNR of the AMFR for the 2 groups of 3-month-olds (tested at 65 dB SPL in Experiment 1 and at 75  
309 dB SPL in Experiment 2) is represented in **Figure 4.B**. The average response for the 8 Hz condition  
310 in Experiment 2 appears to be larger than the average response recorded in the 3-month-old group  
311 from Experiment 1, but there is still no observable averaged response at 40 Hz. The Mann-Whitney  
312 U test comparing 2 independent samples showed a significant effect of Intensity level (65 vs 75 dB  
313 SPL) between the two groups of 3-month-olds in the 8 Hz condition only ( $U = 40.500, p = .002$ ).  
314 There was no significant difference in the 40 Hz condition ( $U=95.000, p = .486$ ). Thus, the AMFR  
315 amplitude in 3-month-old infants was enhanced by the increase in presentation level but only at 8 Hz.  
316 The analysis of the phase locking value provided no further evidence of a significant response at 40  
317 Hz (see Figure A in Supplementary Materials).





318

319 **Figure 4. A.** Grand average (N=15) of the AMFR (in  $\mu\text{V}$ ) for the 8 and 40 Hz condition in the second

320 group of 3-month-old infants stimulated at 75 dB SPL. The data are shown for the Fz channel. **B.**

321 Individual AMFR magnitude (in dB SNR) in 3-month-olds as tested at 65 dB SPL in experiment 1

322 (filled green circles) and at 75 dB SPL in experiment 2 (filled pink circles). Open symbols represent

323 the average of each group and the error bars represents the standard deviation. The horizontal grey

324 dashed line represents the critical value for 0.05 level of significance for the F ratio.

325

326 **IV. DISCUSSION**

327 The goals of the present study were to measure the ability of the auditory system to follow

328 AM cues during infancy while 1) comparing awake infants with awake adults, 2) comparing slow versus

329 faster AM rates. AMFRs were observed in awake 3 and 10-month-old infants for a slow modulation

330 rate of 8 Hz, while at 40 Hz modulation rate we failed to detect a significant AMFR.

331           Infants showed an adult-like AMFR to an 8 Hz sinusoidally modulated-tone. In particular, the  
332 percentage of significant AMFR at 8 Hz resulted in 44% of all participants stimulated at 65 dB SPL  
333 in Experiment 1. This value is consistent with previous studies in adult listeners (Gransier et al., 2020),  
334 observing that less than 50% of participants show a significant AMFR at a rate of 7.5 Hz when  
335 presented at 70 dB SPL. In Experiment 2, increasing the level of sound presentation by 10 dB  
336 increased the AMFR at 8 Hz in 3-month-old infants and increased the percentage of significant AMFR  
337 at 93%. This result reflects effective phase-locking to a modulation frequency which falls in the range  
338 of slow AM that are particularly relevant for speech perception by 3 months of age (Drullman, 1995;  
339 Shannon et al., 1995). Thus, with this finding, we encourage future investigations aiming at a better  
340 understanding of the interaction between auditory development in the AM domain and early language  
341 acquisition. More generally, further investigations are also needed to evaluate cortical tracking of AM  
342 in awake infants with different carriers, as we only used pure tones, and testing more AM rates.

343           At 40 Hz modulation rate, we failed to detect a significant AMFR in awake infants aged 3 and  
344 10 months. Increasing the sound level presentation by 10 dB for an additional group of 3-month-olds  
345 did increase the AMFR for the AM rate of 8 Hz, but still no significant response was observed at 40  
346 Hz. Importantly, as our participants were awake during sound presentation, our results suggest that  
347 the absence of AMFR at 40 Hz in infants is not related to the state of arousal, thus ruling out the  
348 hypothesis that infants' sleep has a suppressing effect on the AMFR at 40 Hz (Levi et al., 1993).

349           The immature phase-locking observed at 40 Hz in infants, as recorded with EEG, is consistent  
350 with previous developmental studies conducted with sleeping infants, that showed a protracted  
351 developmental trajectory for the 40 Hz neural response (Aoyagi et al., 1993; Levi et al., 1993). In  
352 particular, Levi et al. (1993), testing 1-month-old asleep infants at modulation rates between 10 and  
353 80 Hz, showed that the AMFR was not consistently observed for the rates falling below (and  
354 comprising) 40 Hz (the AMFR at 40 Hz was only shown by 4 infants out of 12 tested with a 500 Hz  
355 carrier and by 4 infants out of 14 tested with a carrier of 2000 Hz).

356 One possible interpretation of this absence of AMFR at 40 Hz in young participants could be  
357 that young listeners do not process the faster AM cues as adults, and thus, that the upper limit of the  
358 neural TMTF grows over age. However, it is difficult to endorse this hypothesis. In the first place, it  
359 seems improbable in light of the fact that the Frequency Following Response (FFR) can be measured  
360 in infants (Lemos et al., 2021), implying that infants' temporal resolution must be high. Secondly, it is  
361 not supported by recent behavioral experiments showing similar TMTF in 3-month-old infants and  
362 adults (Walker et al., 2019): in this study, the maximal modulation rate that could be reliably detected  
363 by infants, as estimated using a broadband noise carrier, was 81.7 Hz and was not significantly different  
364 from adults' maximal rate (87.5 Hz). Even though the current experiment used a different kind of AM  
365 carrier than Walker and colleagues (that is, a pure tone, and not a noise carrier), we should expect  
366 higher cutoff frequency for the TMTF without the presence of the inherent envelope fluctuations  
367 carried by a noise carrier in infants and adults (Dau et al., 1997). It is important to note, though, that  
368 ASSR-measured hearing thresholds for a 40 Hz modulated tone have been shown to be about 10 dB  
369 above audiometric, behaviorally-measured hearing thresholds (see Picton et al., 2003). Nevertheless,  
370 our second experiment revealed that increasing by 10 dB stimulus presentation did not influence the  
371 AMFR at 40 Hz for 3-month-old, suggesting that the absence of 40 Hz AMFR observed here in  
372 infants is unlikely to reflect specific processing difficulties at this rate (e.g., hearing or detection  
373 thresholds effects).

374 Alternately, our results may be explained by the neural loci of AM processing for higher modulation  
375 rates changing over development, as a result of brain maturation.

376 In adults, experiments using functional Magnetic Resonance Imaging (fMRI) showed that, even  
377 though slow and faster AM rates activate similar cortical regions (Heschl Gyrus, superior temporal  
378 sulcus and associative areas), specific regions are also activated as a function of the AM rate. More  
379 precisely, fluctuations comprised between 32 and 256 Hz have been found to activate more the  
380 inferior colliculus of the auditory brainstem, while fluctuations of 8 Hz activated more the primary  
381 auditory cortices (Giraud et al., 2000). Using Magneto-Encephalography (MEG) (Weisz and Lithari,

2017) and EEG (Farahani et al., 2017), several studies suggested multiple sources of activation for 40 Hz modulations both at the brainstem and at the cortical level. As MEG and low-density EEG are more sensitive to cortical versus subcortical activity, the absence of 40 Hz AMFR in young listeners may then be related to the development of those cortical regions. Such perspective has been suggested by previous experiments using MEG between 5 and 52 years of age, detecting a significant developmental trend until adolescence for the AMFR at 40 Hz (Rojas et al., 2006). These results were interpreted by hypothesizing that the maturation of the cortical regions involved in the processing of 40 Hz modulations might develop over age, thus making the sources of the AMFR at 40 Hz out of reach for MEG recording. Similar results have also been observed comparing AMFR measured with MEG in 3-to-5-year-old children and adults (Tang et al., 2016). Moreover, EEG studies measuring brain oscillations for visual stimulations in infancy detected gamma band oscillations at precisely 40 Hz, by 8 months of age (Csibra et al., 2000), showing that such EEG rates can be recorded in the infant brain. Future longitudinal assessments of the AMFR should further evaluate the development of neural coding of temporal information at an individual level (allowing, among other things, to investigate its possible relationship with speech and language development)

Overall, our results corroborate the hypothesis that the immature auditory cortex (e.g. Moore, 2002) has a limited capacity, relatively to the adult brain, to process a 40 Hz modulation rate of sounds. This hypothesis needs to be tested in future studies granting localization of the source of the neural signal. A very simple EEG set-up was applied here, based on previous literature, that cannot shed light on this question. Further investigations using high density EEG are warranted to enable source localization of AMFR for slow versus faster AM rate during the early years of development.

Incidentally, this result (in line with previous studies, see John et al., 2004), also casts doubts on the appropriateness of using the modulation rate of 40 Hz for evoked potential audiometry in infants. Concerning the possible clinical applications of AMFR recording in awake infants, the present experiment showed that it is possible to measure AMFR for a 10-min stimulation period while presenting silent animated videos and toys to infants aged 3 and 10 months. The attrition rate was

408 higher for 10-month-olds as compared to 3-month-olds, due to lack of cooperation and signs of  
409 discomfort leading to noisy data (25% excluding parents' interference, vs 6% in 3-month-olds). The  
410 possibility to test awake infants might thus be considered, here circumventing the difficulty to get  
411 infants asleep when they come to the clinic.

412 Finally, the hypothesis of developmental changes in the neural transmission of temporal  
413 information along the auditory pathway (with a transition from relatively more subcortical to relatively  
414 more cortical responses) fits well with the hypothesis that developmental improvements in AM  
415 processing (Cabrera et al., 2019, 2022; Hall and Grose, 1994) might be triggered by increasing  
416 processing efficiency (the central ability to make efficient use of available AM information). In other  
417 words, thanks to a more distributed network, less sensory information might be lost along the auditory  
418 pathway. Higher neural noise (i.e., spikes that are unrelated to the stimulus, see (Sanes and Woolley,  
419 2011), is indeed observed, in infants as compared to adults in the current study, further supporting  
420 this hypothesis. The relationship between processing efficiency and AMFR for higher versus low  
421 modulation rate in infancy deserves further exploration.

422

## 423 V. CONCLUSIONS

424 The present results show similar signal-to-noise ratio for the AMFR at a slow modulation rate  
425 (8 Hz) in both 3- and 10-month-old awake infants compared to adults. Conversely, we did not observe  
426 any response for faster modulations in both infant groups (40 Hz), even when the sound level was  
427 increased to 75 dB SPL for 3-month-old infants. We posit that 40 Hz modulation rates may be  
428 preponderantly processed by subcortical regions in awake infants, while they are processed by both  
429 cortical and subcortical regions in adulthood. This suggests different developmental trajectories of  
430 temporal processing in cortical and subcortical regions as a function of modulation rates.

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435 **Additional information**

436 The authors declare no competing interests.

437

438 **FIGURE LEGENDS**

439 **Figure 1. A.** Waveforms of two pure tones representing the variations in amplitude over time of a  
440 tone modulated at 8 Hz (upper panel) and at 40 Hz (lower panel). A 50-ms on and off ramp was  
441 applied. **B.** Schematic representation of the EEG setup including: the 3 central electrodes used for  
442 AMFR measurement (Fz, Cz and Pz); the ground, as placed at Fpz; the 2-linked mastoids (A1, A2),  
443 used as online reference.

444 **Figure 2.** Grand average (N=15) of the AMFR (in  $\mu\text{V}$ ) for the 8 Hz (left panels) and 40 Hz (right  
445 panels) conditions in the three age groups (3-month-olds, 10-month-olds and adults from the top  
446 panel to the bottom panel, respectively). The data are shown for the Fz channel.

447 **Figure 3.** Individual AMFR magnitudes (in dB SNR) are represented in each group (closed circles in  
448 green, orange and blue for 3-, 10-month-olds and adults, respectively). Open circles represent the  
449 group averages in the 8 Hz and in the 40 Hz condition. The error bars represents the standard  
450 deviation. Higher magnitude corresponds to higher AMFR peaks. The horizontal grey dashed line  
451 represents the critical value for 0.05 level of significance for the F ratio.

452 **Figure 4. A.** Grand average (N=15) of the AMFR (in  $\mu\text{V}$ ) for the 8 and 40 Hz condition in the second  
453 group of 3-month-old infants stimulated at 75 dB SPL. The data are shown for the Fz channel. **B.**  
454 Individual AMFR magnitude (in dB SNR) in 3-month-olds as tested at 65 dB SPL in experiment 1  
455 (filled green circles) and at 75 dB SPL in experiment 2 (filled pink circles). Open symbols represent  
456 the average of each group and the error bars represents the standard deviation. The horizontal grey  
457 dashed line represents the critical value for 0.05 level of significance for the F ratio.

458

459 **SUPPLEMENTARY MATERIALS**

460 See supplementary material at [URL will be inserted by AIP] for a supplementary analysis  
461 of phase locking to AM applied to our data (phase locking value calculated as the  
462 correlation between the phase of the EEG signal and the phase of the input auditory  
463 signal).

464

#### 465 **DATA AVAILABILITY**

466 The raw data will be available upon request to the corresponding author.<sup>ii</sup>

467

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<sup>i</sup> Other measures can also be used to assess the ability of the auditory system to follow the variations of a sound. For instance, the phase locking value can be calculated as the correlation between the phase of the EEG signal and the phase of the input auditory signal (Lachaux et al., 1999; Zhu et al., 2013). However, we calculated those values in the current experiment and found the exact same results as for the AMFR, that is, a strong response in the adult group but an absence of response at 40 Hz in both infant groups (see Figure A in Supplementary Materials).