

Updates in Evoked Potentials: Frequency Following responses: A window to central auditory system.

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Land Acknowledgment



- We pay respect to the Algonquin people, who are the traditional guardians of this land. We acknowledge their longstanding relationship with this territory, which remains unceded. We pay respect to all Indigenous people in this region, from all nations across Canada, who call Ottawa home.
- We acknowledge the traditional knowledge keepers, both young and old.
- And we honour their courageous leaders: past, present, and future

Declaration of interest



No conflict of interest to declare



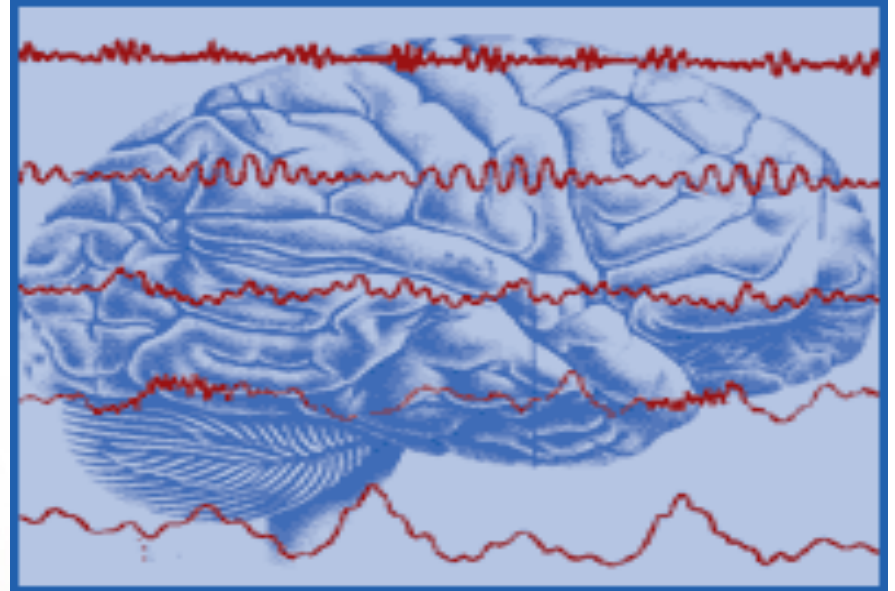
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Plan of my presentation



- Updated in Evoked Potentials:
 - Clinical versus Research
 - Where are we?
 - New tool?
 - Current literature
 - Brain Lab
 - Barcelona's study



Tirée du <http://www.brams.umontreal.ca/cours/files/PSY-6022A2006/DEllemberg>



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What do we know so far?
Where are we?
“Hearing loss detection”



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Introduction:

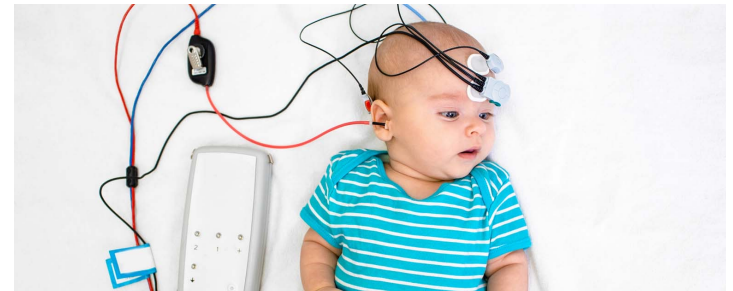
Hearing loss detection/identification

Universal neonatal hearing screening (UNHS), also known as early hearing detection and intervention program (EHDI):

Identification, intervention, and follow-up of newborns with congenital deafness and hearing loss.

Performed worldwide
otoacoustic emissions (OAE)
automated auditory brainstem responses (AABR)

Different protocols based on the risk factors



<https://www.audiology.org/could-newborn-hearing-screenings-be-used-to-identify-children-with-autism-spectrum-disorder/>

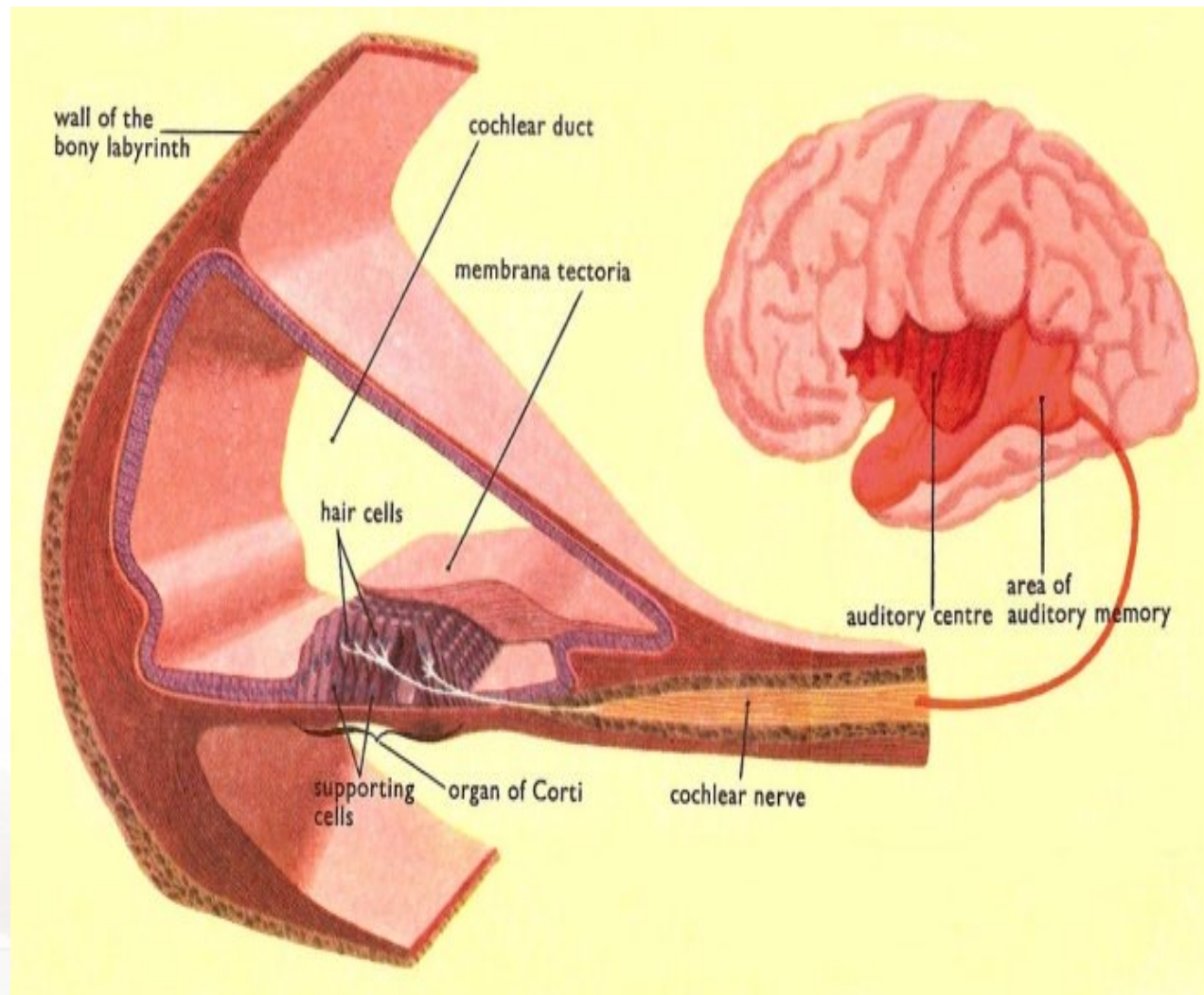


Is it enough?
It depends on.....



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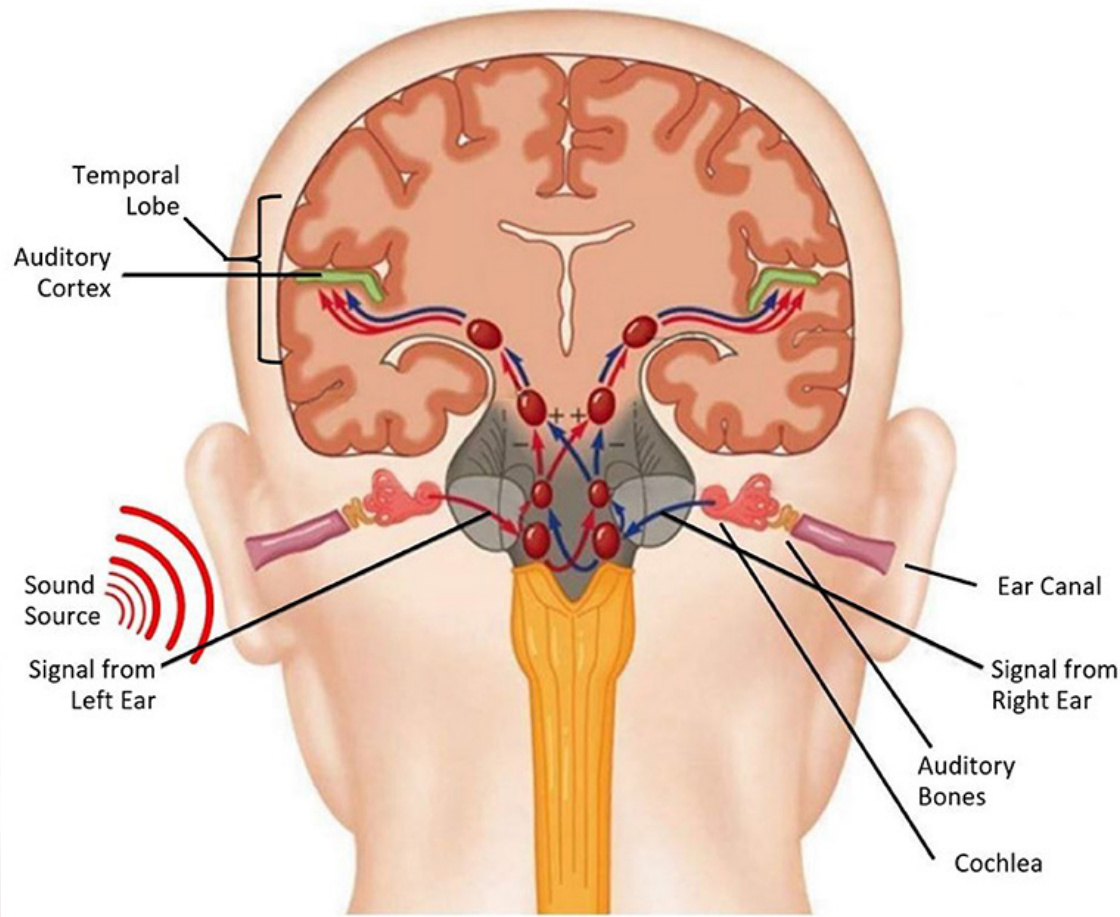
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www.daviddarling.info/.../O/organ_of_Corti.html



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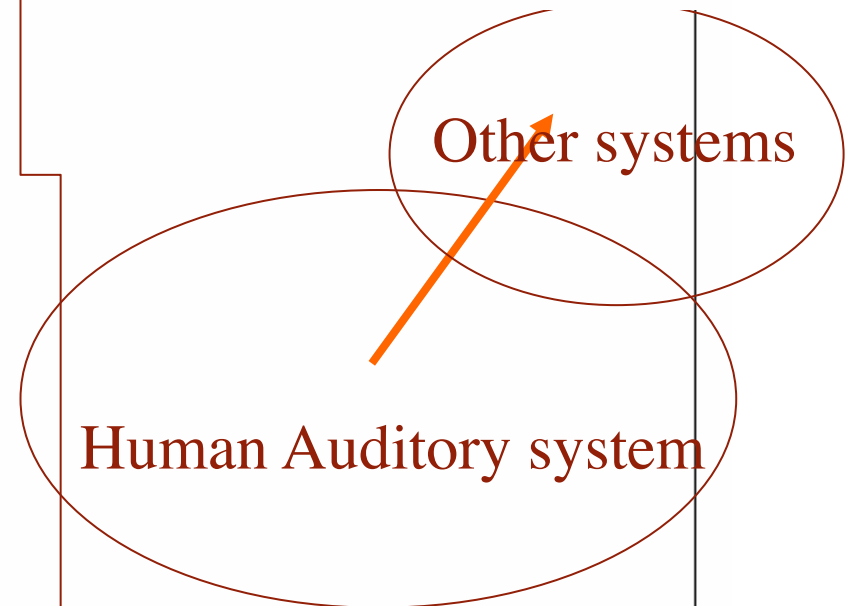
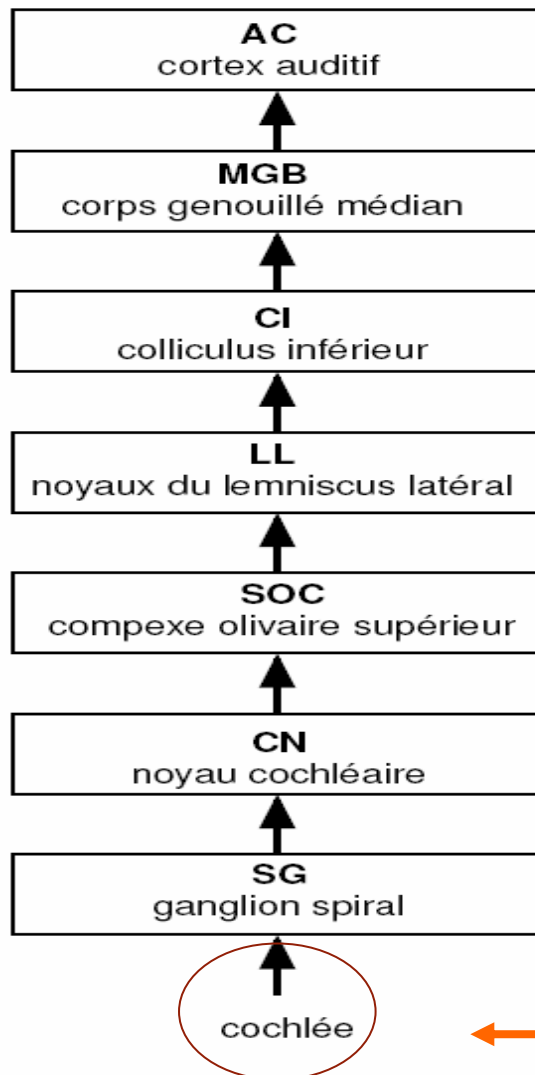
Son → Oreille → Cerveau

(système auditif
périphérique)

(système auditif central)



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(CISG-SLPA, 2012; Millet et al., 2012)

Hiérarchie ascendante des principaux niveaux du système nerveux auditif.



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**Is it enough to detect the
presence of sound?
It depends on.....**



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Is it enough?



Children who were born healthy and passed the UNHS could have

neurodevelopmental delays/disorders (autism)

deficits in language acquisition, reading comprehension, reading acquisition, dyslexia, specific language disorders, auditory processing disorders, etc

consequent impact on their cognitive function and emotional regulation, and the corresponding socioeconomic negative impact.



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Current clinical situation



To date, there is a lack of objective procedures for
early detection of newborns at risk for Listening/language processing difficulties during the first moments of life

The identification of these disorders occurs when
No expected typical behavior ? or
displays an altered or deficient behavioral pattern

Hope / Dream

to detect a potential language/central auditory
impairment at birth in a similar manner as
congenital deafness



Potential clinical measure/tool ?



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Potential clinical measure/tool ?



- Objective, familiar
- Can be recorded with **a similar equipment** used in the AABR test of the UNHS.
- Continuous efforts to improve the quality of hearing assessments have led to increased interest in new stimuli (the rich acoustic information) and modalities,
 - **such as use of speech in electrophysiological recordings or speech ABRs and, more particularly, the second part of the speech ABR, referred to as the “frequency-following responses” (FFRs to the speech).**
- Produced by the **synchronous activity of neurons of the subcortico-cortical network**

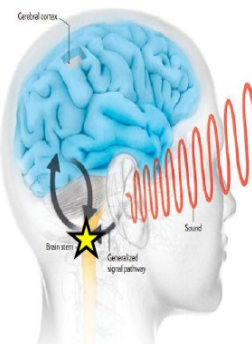
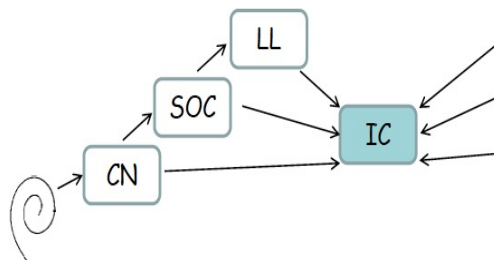
Bidelman, 2018; Chandrasekaran & Kraus, 2010; Coffey et al., 2017, 2019.

Potential clinical measure/tool ?

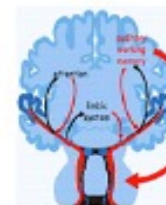
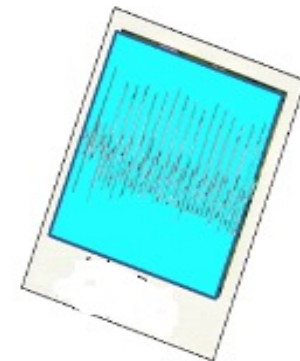
FFR to speech sound



- The FFR reflects the capacity of encoding the temporal and spectral features of speech (Coffey et al., 2019)
 - Provides a window to explore the integrity of the auditory pathway beyond the mere transmission of sound



a snapshot



of auditory processing

<http://www.soc.northwestern.edu/brainvolts/>



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What is FFR



FFRs can be recorded noninvasively from the scalp with electroencephalography (EEG) and magnetoencephalography, and emerge between 7 and 15 milliseconds from sound onset to auditory frequencies in the range of 100 to 1,500 Hz.

FFR is a sustained and periodic auditory evoked potential that reflects synchronous neural phase locking to the spectrotemporal components of the acoustic signal in the ascending auditory system.



Is it S-ABR, c-ABR, FFR, ASSR, subcortical responses etc?



- This neural response has been termed throughout the literature with other names that have been used interchangeably or which highlight a specific aspect or variant of the response. These include S-ABR, c-ABR, FFR, ASSR, subcortical responses
- The scientific community has agreed that the term “FFR” is the most accurate one, as it refers exclusively to what the component is: a response that follows the frequencies of the incoming stimulus.



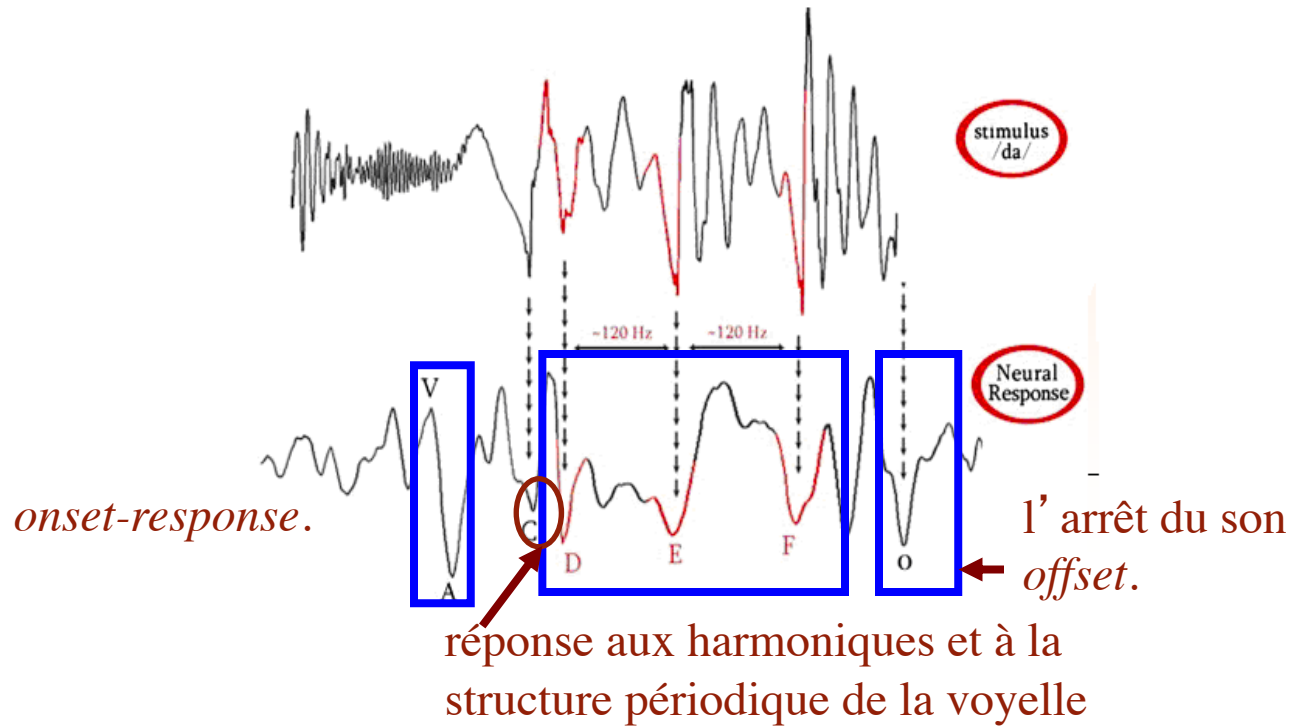
FFR to speech sound



- The FFR has great potential **to answer both basic and applied questions** about the processes involved in sound encoding, language development, and communication.
- It can be obtained through **passive and active listening paradigms** and, by decomposing the recorded signal into **temporal and spectral domains**.
 - (e.g., detection and tracking of the fundamental frequency [F0] and harmonics; e.g., Krishnan, 2002).
- It provides an objective indicator of the fundamental acoustic features intrinsic to speech sounds, including
 - **time (onset & latency),**
 - **pitch (fundamental frequency, F0), and**
 - **timbre (the harmonics)**

Krizman & Kraus, 2019; Skoe & Kraus, 2010

40 ms /da/

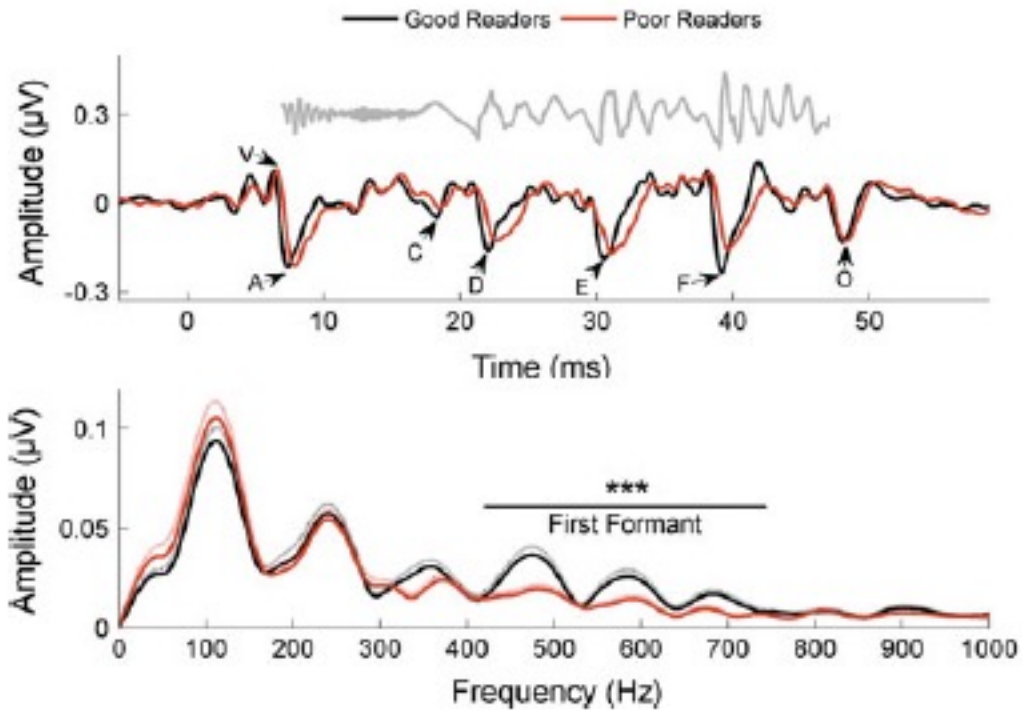


Kraus N, Nicol T, Zecker S, Skoe E. Auditory Neuroscience Laboratory, Northwestern University



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40 ms /da/



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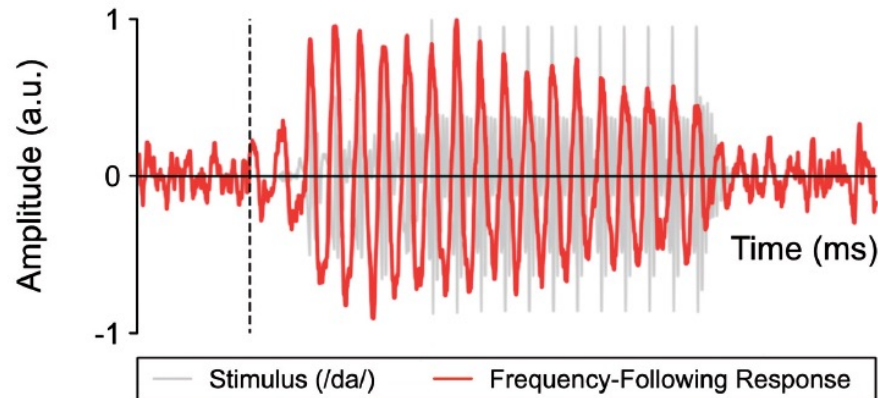
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FFR

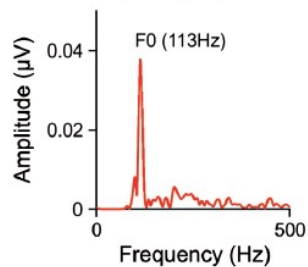
170 ms /da/



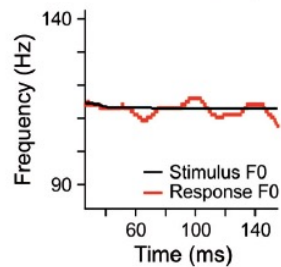
Time Domain



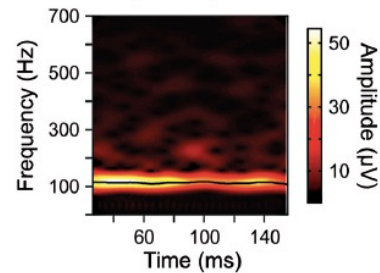
Frequency Spectrum



Pitch Tracking



Spectrogram



FFR Analysis



FFR allows

- studying the latency and amplitude of the neural response elicited to incoming sounds in the **time domain**.
- analyzing **the frequency components of the neural response** in the spectral domain, the magnitude with which the fundamental frequency and harmonics have been encoded (Fig 170 ms da).

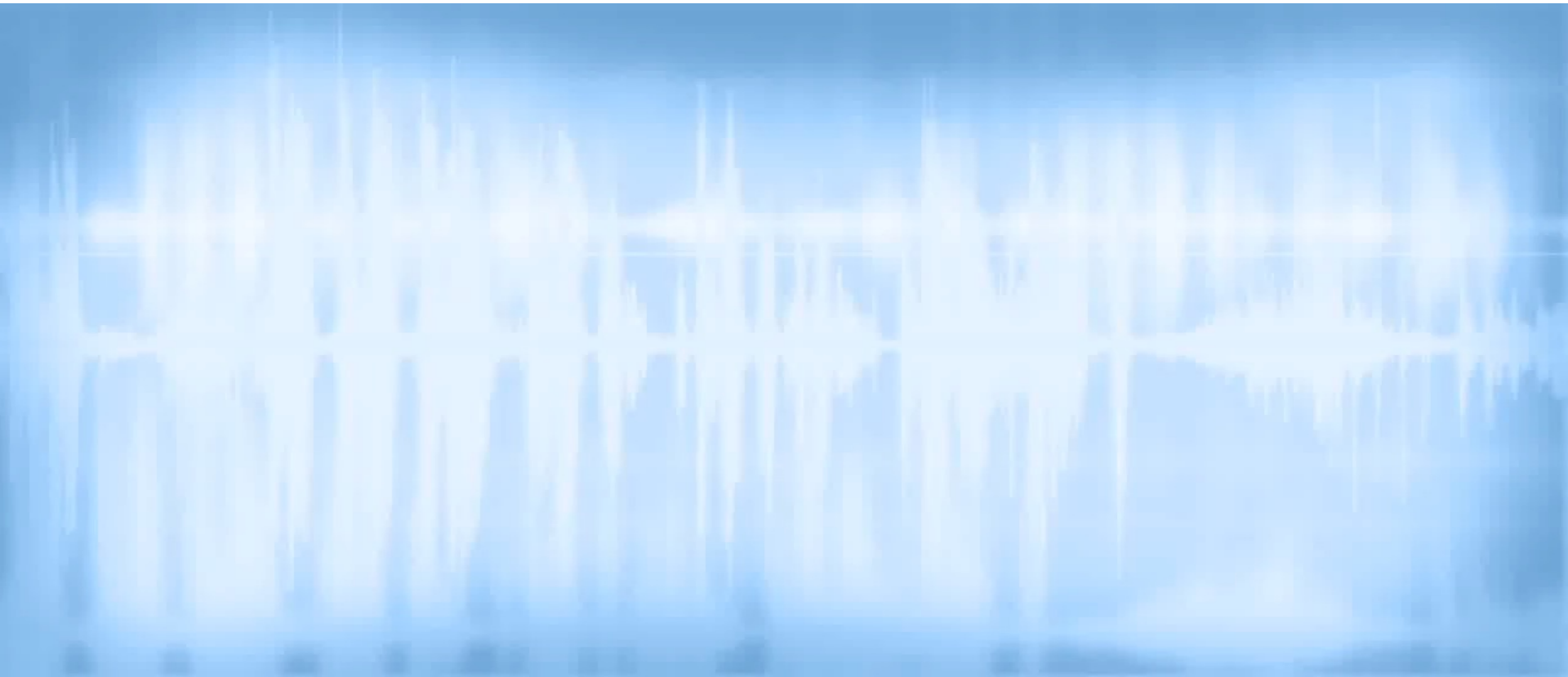
The analysis

- How **well subcortico-cortical network neurons track temporal** (phase locking) **and frequency** (neural phase locking at the pitch period) characteristics of different stimuli (Krizman & Kraus, 2019; Skoe & Kraus, 2010)
- Provides a window to understand
 - **experience, context, and challenging conditions, such as listening in noise, age, and speech and language disorders.**

Short Video



- https://www.youtube.com/watch?v=qEQuM_rpI6I&t=72s



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Review Article

Characteristics of the Frequency-Following Response to Speech in Neonates and Potential Applicability in Clinical Practice: A Systematic Review

Céline Richard,^{a,b}  Mary Lauren Neel,^a Arnaud Jeanvoine,^a Sharon Mc Connell,^a Alison Gehred,^c and Nathalie L. Maitre^{a,d}



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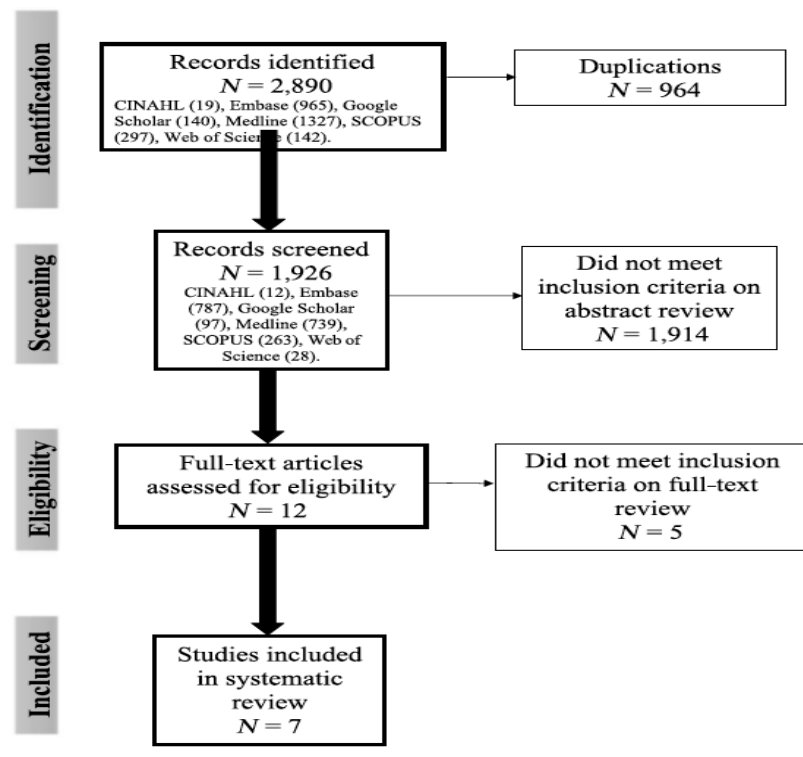
Important clinical questions



1. Can the FFR in response to speech be performed in newborns with an easy, rapid methodology at infant bedside in the nursery?
2. Can stimuli used to elicit the FFR be universally valid, even across cultures and languages?
3. What quantitative information on speech processing will the neonatal FFR provide?
4. Can the FFR in response to speech provide normative data with regard to speech perception and maturation at either cohort or individual levels?
5. Does the FFR have validity in clinical use for diagnosis, early intervention/rehabilitation, and follow-up?



Figure 1. PRISMA-based flowchart of articles selection. CINAHL = Cumulative Index to Nursing and Allied Health Literature.



Important clinical questions



1. Can the FFR in response to speech be performed in newborns with an easy, rapid methodology at infant bedside in the nursery?
 - Yes: with minor modification (ex: More sweeps, REA, binaural is better)
2. Can stimuli used to elicit the FFR be universally valid, even across cultures and languages?
 - Yes: 40 ms and or 170 ms /da/
 - other stimuli as well



Important clinical questions



3. What quantitative information on speech processing will the neonatal FFR provide?

- tracking of voice pitch encoding
- neural phase-locking magnitude
- Other important processing information

Important clinical questions



4. Can the FFR in response to speech provide normative data with regard to speech perception and maturation at either cohort or individual levels?

- Normative data regarding neonatal FFR were collected both at the cohort and individual levels.
- Maturational changes within the first 3 months of life.
- **Major limitations.**
 - Cohort size in this review, with four studies having a very limited number of subjects.
 - variability between subjects
 - limited prenatal history



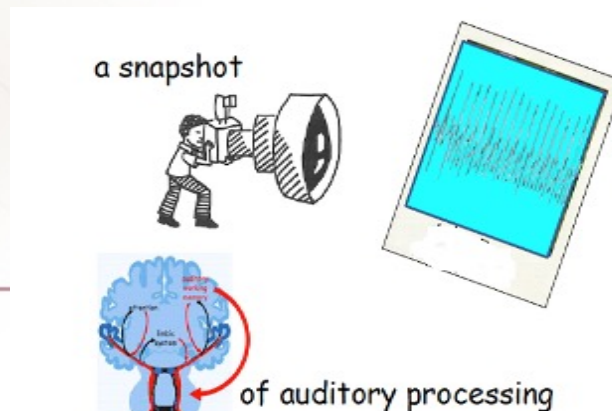
Important clinical questions



5. Does the FFR have validity in clinical use for diagnosis, early intervention/rehabilitation, and follow-up?

Current evidence suggests that the FFR could be **a promising tool in the objective evaluation of speech representation** in the **neonatal subcortico-cortical network**.

It provides **an essential snapshot of neurophysiological markers of speech processing in children**.



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TECHNICAL ASPECTS FOR OBTAINING A NEONATAL FFR: STIMULATION, RECORDING, AND ANALYSIS PROCEDURES



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Table 1 Recommended Preparation and Recording Parameters to Record Neonatal and Adult FFRs

Preparation	Recommendation	Rationale
Adults	Recording performed in an electrically and acoustically shielded room	Recording carried away from any type of electrical and acoustical interference
	Participant instructed to relax and not move during the recording. Instructed to blink at a normal pace and eye activity recorded with a vertical and horizontal electrooculogram	Avoid possible muscle movements that could contaminate the recording
	Clean the facial area where electrodes will be placed with (1) alcohol, (2) abrasive gel, and (3) alcohol again	Important to remove sweat, makeup, and other residuals that might be on the skin. The second cleaning with alcohol is important to remove all the rest of abrasive gel and avoid causing irritation when placing an electrode on top of it
	After the recording, remove the electrodes using a gauze or a cotton pad soaked with alcoholic solution or using an adhesive remover such as Niltac	Remove the facial electrodes with minimum harm
Newborns	Recording performed in the hospital room at the maternity ward, with the baby in its crib or in the mother's bed without skin-to-skin contact	Recording carried away from any type of electrical interference, including the electricity from the adult's own skin. If the bed is electrical, it is recommended to be disconnected
	Participant sleeping throughout the whole FFR recording. It is recommended that the recording is performed ~15 minutes after feeding to ensure a deep sleep	Avoid possible muscle movements that could contaminate the recording
	Clean the facial skin area where electrodes will be placed with (1) abrasive gel and (2) alcohol or saline solution	Remove residual substances from birth. Especially important as newborns can still have vernix caseosa on the skin





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Neonatal Frequency-Following Responses: A Methodological Framework for Clinical Applications

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Sonia Arenillas-Alcón, M.Sc.,^{1,2,3} Marta Puertollano, M.Sc.,^{1,2,3}
M. Dolores Gómez-Roig, M.D., Ph.D.,^{3,4} and Carles Escera, Ph.D.^{1,2,3}**



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Auditory brainstem response to complex sounds: a tutorial

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Analyzing the FFR: A tutorial for decoding the richness of auditory function

Jennifer Krizman¹, Nina Kraus^{1,2,†}



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Effects of background noise on the encoding of speech sounds in neonates:

A frequency-following response (FFR) study

Koravand A., **Alejandro Mondéjar-Segovia**, Llobet-Gil, R., Arenillas-Alcón, S., Costa-Faidella, J., Konczol, A., Ribas-Prats, T., Gómez-Roig, C., & Escera, C



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Background



- Infants and young children need **a greater SIN ratio** than adults (Erickson & Newman, 2017; Sobon et al., 2019; Leibold et al. 2019; Leibold et al., 2016).
- **Learning difficulties have also been associated with a stronger vulnerability to noisy environments** (Bradlow et al., 2003).
 - For example, children and young adults with autism spectrum disorder (ASD) (Alcántara et al. 2004), dyslexia (Dole et al., 2012) or specific language impairment (Ziegler et al., 2005; Ziegler et al., 2011) **have significantly poorer speech perception in noise** compared to typically developing children.
- This difficulty can be exacerbated by developmental deficits during the first years of life and can eventually lead to language difficulties.

Background



- Studies focusing on the neurophysiological basis of SIN processing have suggested that the worsening influence of noise in speech processing **may result from the interference of speech encoding at the brainstem level** (Anderson & Kraus, 2010; Song et al., 2011; White-Schwoch et al., 2015).
- Speech-in-noise FFR responses have been studied in adults and in children with normal and/or abnormal SIN processing (Anderson & Kraus, 2010; Song et al., 2011; White-Schwoch et al., 2015, Presacco et al. 2016, Koravand et al, 2019)

Important elements



- FFR reflects the encoding of temporal and spectral features of speech sounds and is disrupted in a wide range of language-related disorders.
- The effect of background noise on speech processing during the earliest stage of life has not been investigated using FFR.



Objectives



to explore the possibility of using FFR as a potential biomarker for measuring speech in noise (SIN) in babies.

More specifically: to document the feasibility of recording FFRs in babble noise in neonates within a maternity ward during the days immediately after birth and to compare this effect against that from a reference group of adults.



Hypothesis



Based on recent finding regarding early speech in quiet perception in newborns (Ribas et al., 2019) and SIN perception in infants (Musacchia et al, 2018), we hypothesized

1. Newborns would obtain consistent **FFRs to speech in quiet and in a noise.**
2. A **greater background noise effect on F0 encoding in newborns** than in adults. This effect would be expressed strongly during the consonant transition region

Method



- **Participants:**

- 25 healthy term newborns (14 females; aged 30.67 ± 2.85 hours after birth) recruited from the Sant Joan de Déu Children's Hospital in Barcelona (Catalonia, Spain)
 - Exclusion criteria : Apgar score, passing UNHS, no complication during the birth
- 25 adults (15 females, aged 27.32 ± 1.08 years) were recruited from the University of Barcelona.
 - No history of psychiatric or neurological disorder, nor hearing impairments

Method



- Preceding FFR recording
 - wave V. ABR was obtained by using a standard click of 100 μ s square-wave click presented at 65 dB sound pressure level (SPL) in both age groups.
- FFRs were recorded to **/da/ syllables in quiet and in ipsilateral babble noise** for the latter (S/N= +10), respectively.
 - /da/ syllable with a duration of 170 ms and a fundamental frequency (F0) of 113 Hz
 - **The /da/ syllable is divided into three segments:**
 - an onset period of 10 ms,
 - 47 ms consonant transition (10-57 ms)
 - 113 ms of steady vowel section (57-170 ms).

Method



- The **noise condition** was assessed by playing **a Spanish six-talker babble noise (4 females and 2 males, 75 s track) at 55 dB SPL** (at 10 dB attenuated intensity)
- **Rate of 3.7 Hz** with an inter-stimulus interval of 100.27 ms.
- **Alternating polarities** to the **right ear** through ER3C Etymotic shielded earphones of 300 Ω (ER, Elk Grove Village, IL, EEUU) connected to a Flexicoupler adaptor (Natus Medical Incorporated, San Carlos, CA) in newborns, and to a custom-made earcup in adults.



Method



Data acquisition

- Stimuli were delivered using a SmartEP platform including the cABR and Advanced Hearing Research modules (Intelligent Hearing Systems, Miami, FL, EEUU).
- **Six blocks of 1000 /da/** repetitions were presented in two different conditions (**three blocks per condition**): quiet and noise.
- The noise condition consisted on the simultaneous presentation of the /da/ stimulus and the babble stimulus.
- Auditory conditions were alternated to reduce possible neural adaptation.

Data acquisition



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Babies Data Acquisition



- Neonatal FFRs were recorded while **neonates were sleeping in** their bassinets at their hospital rooms.
- Recording was paused at any sign of wakefulness or movement, cancelling it if sleep could not be restored.



Babies Data Acquisition



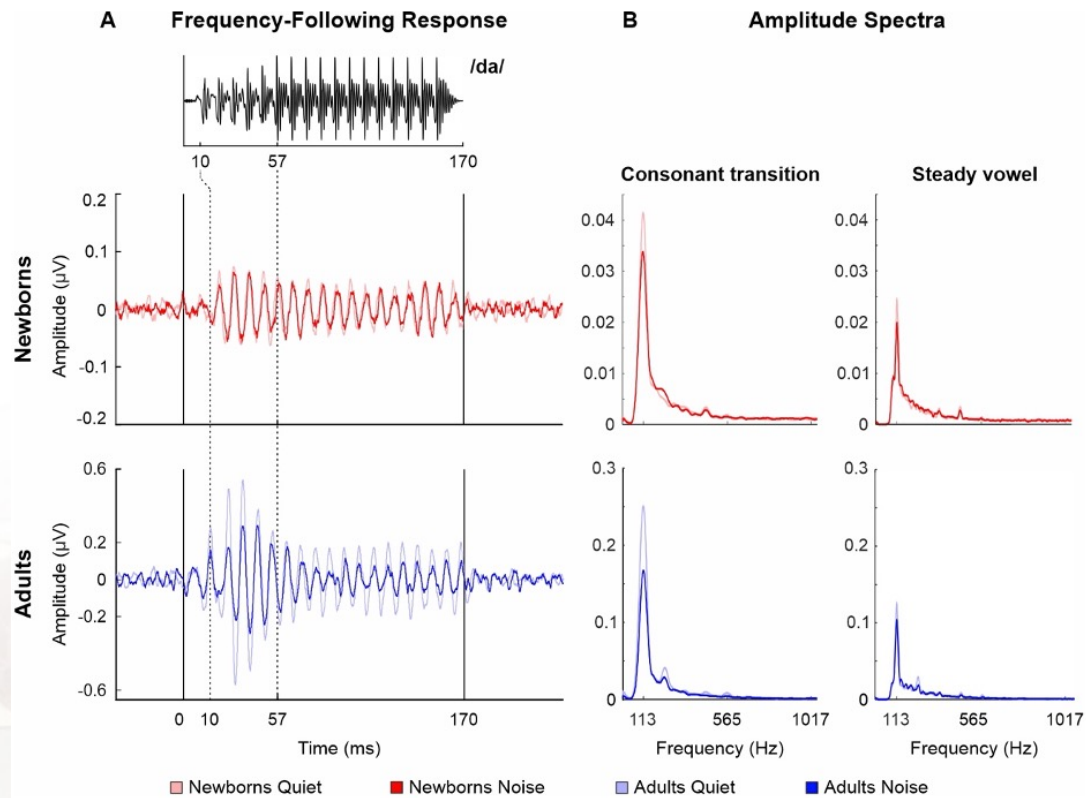
- Total duration of the recording was approximately **38.80 (\pm 1.14) minutes**
 - (two click blocks \times 2000 sweeps \times 51.81 ms SOA, plus six /da/ blocks \times 1000 sweeps \times 270 ms SOA, plus the duration of rejected sweeps).
 - Additional 5 minutes were spent in the preparation time, including electrode positioning, checking for impedances and electrode removal.
 - The average time also included the time necessary to recover sleep in cases where the recording session was interrupted by demonstrated discomfort or sleep disturbance in the newborns.

Method: Data pre-processing and analyses



- The continuous EEG signal was acquired at a sampling rate of 13333 Hz, applying an online bandpass filter from 30 to 1500 Hz and dividing it into epochs of 270.27 ms (including 40 ms of pre-stimulus baseline).
- Three FFR parameters were retrieved from the recordings in time and frequency domains for both sections of the stimulus (**Consonant transition and steady vowel**) separately.
 - Root mean square [RMS] of the prestimulus region,
 - Signal-to-noise ratio [SNR] of the brain response,
 - Spectral amplitude.

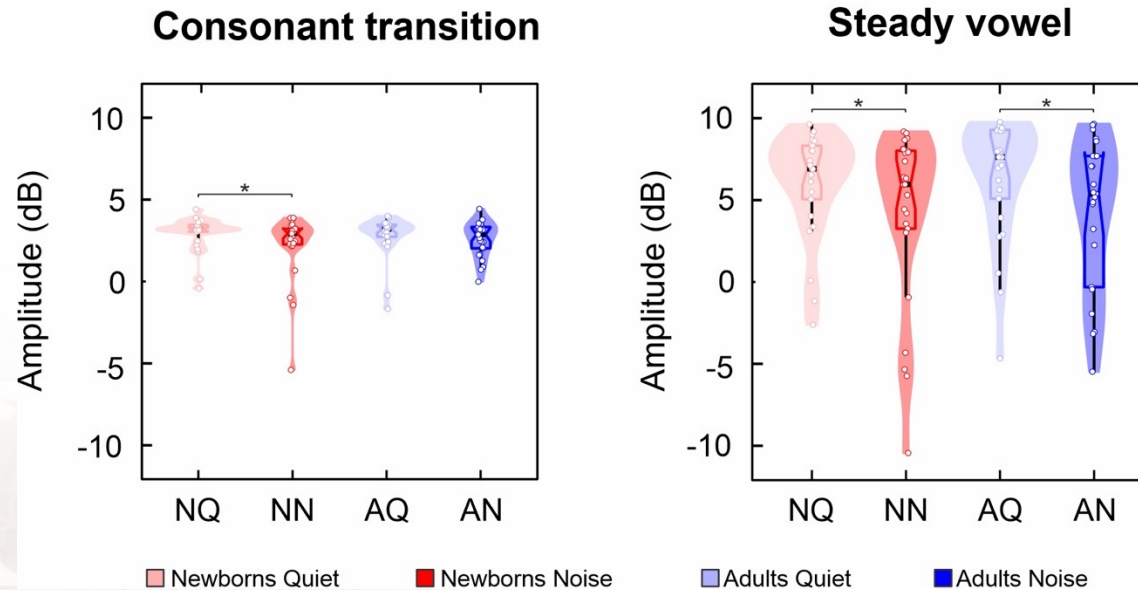
Results



Results



SNR for the F0



Results



Newborns obtained reliable FFRs to speech in quiet and in background noise;

Both newborns and adults exhibited larger signal amplitude to the speech stimulus in silence than when presented in noise

Newborns obtained overall lower values than adults in all parameters except the vowel SNR of the response;

FFR was affected by noise during the consonant transition in two groups.

Newborns experimented the effect of noise in the steady vowel section as well.

Discussion



- Findings suggest that newborns process speech presented in background noise at birth differently, possibly due to their immature auditory system which is exposed to attenuated sounds during gestation.
- This study constitutes the first step towards understanding the development of speech-in-noise (SIN) processing from the first days of life.
- An early detection of FFR abnormalities in processing SIN could lead to earlier intervention of central auditory processing disorders and language difficulties.

Limit of the study



1. Different state of alertness, when sleeping newborns are compared with awake, relaxed adults with their eyes closed, may be a factor contributing to the observed group differences.
 - a. attentional modulations of the cortical generators of the FFR (Coffey et al., 2019, 2016; Hartmann and Weisz, 2019)
 - b. the extent to which subcortical sources of the FFR are modulated by attention is not well established (Hartmann and Weisz, 2019).



Limit of the study



- The presentation intensity
 - Adults versus babies



CONCLUSION



SIN processing can be studied at birth.

Newborns can perceive speech syllables in quiet and noisy environments.

Newborns present impoverished neural encoding of speech in background noise conditions from the very first moment from birth.

Even though, the pattern of disruptions in the neural encoding of speech was different from the adult one, the sensitivity to noise was similar.



Conclusion



This study aims to promote the need for future longitudinal research using FFR in early developmental stages to assess SIN encoding, pursuing to elucidate whether it could become **a predictive biomarker of future auditory processing deficits** and, consequently, **certain language-related disorders.**

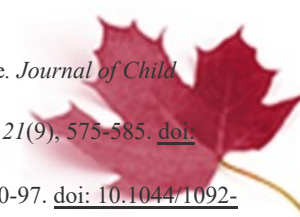


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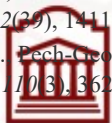


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Many thanks
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Questions?



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