Nature vs nurture in newborn voice perception. An fMRI comparison of auditory processing between premature infants at term age and term born neonates

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Introduction

One of the most exciting challenges in developmental neurosciences is to investigate the influences of innate and experience-dependant brain development. To date, only few fMRI studies have however focused on the development of brain functions such as language and cortical vision in neonates as well as in young infants (e.g. [1] [2]). On the other hand, prior data evaluating the human cortical folding have demonstrated the differential maturation of the superior temporal sulcus in the right hemisphere with respect to the left one [3]. This asymmetry could reflect early hemispheric functional specialization, for instance for human voice recognition, which is attributed in the adult brain to the "what" pathway of the right auditory cortex [4].

We thus designed an fMRI experiment to compare in two groups of neonates (premature infants at term corrected age and term born neonates), the activations elicited when hearing own mother s' voice. The rationale was that premature infants, who have been directly exposed for several weeks to their mother's voice compared to term born neonates, with only a few days of direct voice exposure, would alter their functional brain development due to this stimulating experience.

Methods

Subjects and stimulation. The study was approved by the ethical committee of the Geneva University Hospitals and informed consent from the parents was obtained. Two groups of 6 neonates of both sexes were included: premature infants (mean postnatal age 12.1 ± 1.7 weeks) and term born infants (mean age 0.6 ± 0.5 weeks). Both groups were scanned during the 40th week of post-conceptional age. Cardiac frequency and blood oxygen saturation were monitored. Auditory stimulation was administrated by means of MR compatible earphones. Four different conditions of stimulation were applied in a pseudo-randomized design (2-3 runs x5 alternating epochs of 24s). Conditions were: 1- the mother's voice while she speaks a typical everyday life sentence to her baby (PROPER condition), 2- the reversed unintelligible sentences (from the still recognizable mother's voice – REVERSE condition), 3- the sentences being phase modulated, a manipulation that avoided further voice recognition while keeping the same basic frequencies (NOISE condition), 4- no additive stimulation, only the background attenuated scanner noise (-20db) as in other conditions (REST condition). A majority of subjects were in light, natural sleep, without sedation during most of the experiment.

MR acquisition. Experiments were performed on a Siemens 3T Trio, using a GRE EPI sequence covering the whole brain (30 axial 3mm slices, TR/TE/flip = 2s/30ms/85°, FOV: 200mm, matrix: 128x128mm) and a high resolution T2 sequence for anatomical reference and subsequent normalization.

Data analysis. Post-processing was performed with SPM5 [5]. Time series were unwarped to correct for geometrical distortion, realigned to the first volume, normalized to a home-made template based on a mixture of 20 brains from both premature and term born neonates, smoothed and high-pass filtered. Blocks or runs that exhibited strong movements were discarded from the analysis (almost 20% of the images). Data from every subject could finally be used. Fixed-effect statistical analysis according to the general linear model was performed ($p<.001$, 25 contiguous voxels).

Results and discussion

Common activations. Conjunction analysis reveals several shared activations between the two groups (Fig. 1). First, *every auditory stimulation vs REST* contrast underlines the activation of primary auditory area as expected (coronal slice), whereas secondary auditory areas and associative temporal cortex were activated within the left hemisphere only. Second, the conjunction of *(PROPER & REVERSE) vs NOISE* (hearing mother's voice notwithstanding its intelligibility) yields an activation focus in the right anterior superior temporal gyrus (purple focus in axial slice). This is in complete agreement with fMRI findings on human voice perception in adults [4]. Of interest for the PROPER vs REVERSE conjunction analysis, none activation was found, hence suggesting no common high level processing regions for both groups.

Premature infants-specific activations. Activations in premature infants (Fig. 2) show higher BOLD activations compared to term born neonates (not illustrated). Between group comparison for *every auditory stimulation vs REST* contrast demonstrates the involvement of motor and somesthetic regions (blue), hence suggesting more sucking reflexes and associated motor activity in the premature population. More important, the same comparison for the *(PROPER & REVERSE) vs NOISE* contrast yields a selective activation in the anterior part of the superior temporal cortex (purple), suggesting a possible recognition of mother's voice, as shown in adults [6]. The most striking result in the premature infant group is the differential activation in the *PROPER vs REVERSE* contrast located in the left posterior superior temporal gyrus (hot scale). It underlines the involvement of the so-called Wernicke's area known to be part of phonological decoding in adults [7]. It should be stressed that left temporal activation during language processing has been demonstrated in previous studies on 3m old children born-at-term [1,8].

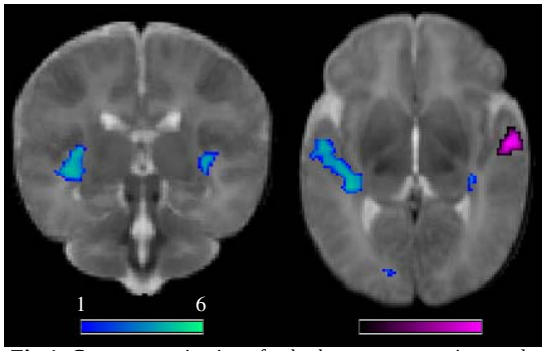

***Fig 1. Common** activations for both groups, superimposed on a template brain from premature and term born infants*
Cold scale: (PROPER & REVERSE & NOISE) vs REST
Purple scale: (PROPER & REVERSE) vs NOISE

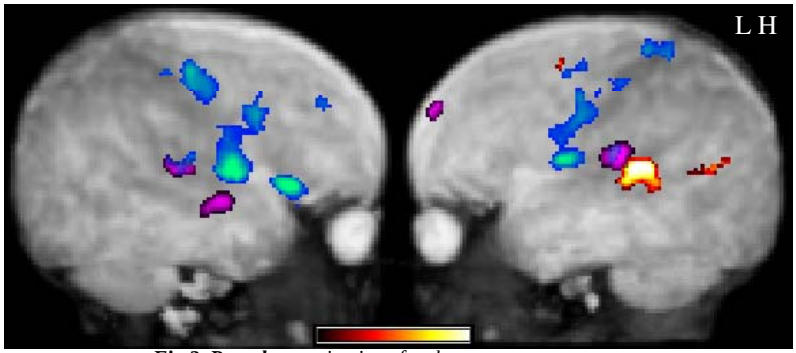

***Fig 2. Prevalent** activations for the **premature** neonates*
Cold scale: (PROPER & REVERSE & NOISE) vs REST
Purple scale: (PROPER & REVERSE) vs NOISE
Hot scale: PROPER vs REVERSE

Conclusion

We currently report novel findings indicating that voice perception is surprisingly well-developed in the newborn (see [4,6] for comparison with adults). When comparing the substrates of auditory processing in premature and term born groups of neonates, different activations were elicited during hearing/listening to complex stimuli, such as voice and reversed voice. Furthemore, prematurely born infant clearly differentiates between mother's voice and reversed mother's voice in cortical regions associated with language processing. Thus, despite well-described delays in its structural development [9], a premature brain seems to experience functional changes oriented on both auditory recognition and language decoding.

References

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