Neuroplasticity in Neonates –
An fMRI Study of Language Stimulated Auditory Activation.

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With an overall objective of establishing a physiologic measure of neuroplasticity in infant human brain, fMRI studies were conducted to isolate regions of the brain specific for phoneme processing and language processing. The neuronal auditory response to 20 sec blocks of noise, human-produced nonsense speech, and short meaningful phrases in the infant's mother tongue was studied in 5 sleeping neonates. Strong activity was observed in Broca's and Wernicke's area, with bilateral activity seen in the primary auditory cortex, with a strong left hemisphere bias. The results indicate that infants show lateralized activation in language areas in response to speech, suggesting that language lateralization is innate and established from birth.

Introduction:

The long term goal of this project is to assess neuroplasticity of injured human infant brain, allowing for recovery after injury of important brain regions. In order to assess the effect of cognitive/sensorimotor intervention, objective physiologic measures, which can quantify consequential enhancement of neuronal activation and sensorimotor function need to be developed. FMRI, an ideal non-invasive tool to investigate such neuronal response, was utilized in the present study to address one of the major controversies in the language literature which concerns the development of left hemisphere laterality for language. This is the first part of a longitudinal study. In a later part, 50% of patients recruited would have undergone some mode of therapeutic intervention including training of the mothers to instill language, motor and verbal skills.

Materials and Methods:

Five neonates, four to eight weeks post discharge were recruited subsequent to obtaining consent (IRB approved) from parents. Inclusion criteria required documented brain asphyxia, seizure or prolonged acidosis.

MR Imaging was performed on the neonates on a 1.5T GE 5X scanner. No sedation was utilized for the babies. They were fed about ~30 to 40 minutes before the scan, put into a "swaddle" bag, which when pressurized wrapped the baby in its own contour. Subsequently, the baby was comfortably wrapped, and lights dimmed to induce sleep. While in the scanner, all vital signs were monitored. Two sets of sound-insulating ear muffs were utilized, which insulated the sounds of the EPI to about 65%, but allowed transmission of the auditory stimuli. The scanning protocol consisted of first a 3D set of thin contiguous (FGRE) slices, acquired for morphometric estimates. This was followed by a set of thin slice T2-wtd FSE images, essentially for clinical diagnostic process. In some subjects, DW images were also acquired. The EPI fMR imaging was preceded by a manual gradient shimming in order to reduce artifacts. The parameters for the GE EPI scan were 18 FOV, 128x64 matrix, TR/TE=2500/60ms, 5mm Thk, Interleaved, 1 Nex. 10 slices with 48 phases per slice were acquired in a total of 2 minute.

Within this two minute scan time, the auditory stimuli paradigm, recorded on an audio tape and played through the headphones during the scan, was utilized for this fMRI study. It consisted of 20 seconds each of: <<(scanner noise)- (normal nonsense speech) – ("motherese" speech) – (scanner noise) – (normal nonsense speech) – ("motherese" speech)>>, yielding 480 images. Motherese speech is deeply intoned, prosodic speech that a mother speaks to her child in the mother tongue (English or Spanish). Standard procedures were utilized for statistical analysis of activated pixels, for the purpose of which we only compared speech to rest. Temporal cross-correlation of the MR signal intensity in each voxel, with the expected rise and fall during task-rest periods, mediated by the known slow hemodynamic blood-flow response, was performed. A cutoff value of 0.30 for Pearson's r statistics (corresponding to a P value of < 0.01) in six or more contiguous voxels defined activated regions.

Results and Discussion:.

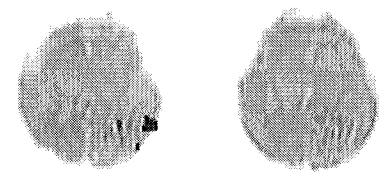

Fig. 1.

The first figure shows inferior slices covering the middle temporal gyri and superior temporal sulcus in Brodman's area 21/22, where Wernicke's area is found in normal adults.

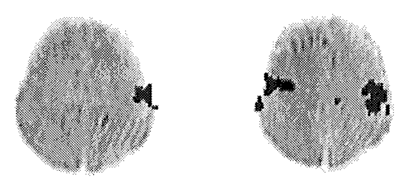

Fig. 2.

The second figure shows two slices through the transverse temporal gyrus and superior temporal gyri.

Strong activity was detected in Broca's and Wernicke's area during human speech. While bilateral activity was observed in the primary auditory cortex, there is a strong left hemisphere bias. In the posterior superior temporal lobe, activity was found solely in the left hemisphere. There was minimal inferior frontal gyrus activity but this may be due to our slice location. Wernicke's area had unilateral activity.

The results indicate that infants show lateralized activation in language areas in response to speech, suggesting that language lateralization is innate and established from birth.

The equipotentiality model holds that both hemisphere begin as capable for supporting language, and left hemisphere bias develops in childhood. This model is supported by data indicating that individuals with early onset lesions of the left hemisphere can develop relatively normal language in the right hemisphere. Models proposing innateness of language dominance posit that the left hemisphere is pre-wired for language, and the right hemisphere cannot fully support language. Evidence for strong laterality in Wernicke's area suggests that left hemisphere dominance is established at birth. We found no activity in the inferior frontal gyrus, and area associated with language expression. It is possible that lateralization of frontal-mediated language expression regions may develop with age, but our data indicate that, at least in language comprehension regions, lateralization of language is already apparent at birth.