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Goals

- 1) Employ an improved experimental paradigm and improved analyses to more accurately determine the major areas involved in auditory deviant detection
- 2) Determine the best degree of location weighting to constrain the inverse solution in order to provide a higher level of sensitivity and specificity in terms of localizing the sources of the ERPs of interest

Methods

- Simultaneous EEG & fMRI
- 17 neurologically normal subjects
- Auditory oddball paradigm with pure tones stimuli
- 320 tone sequences were presented
- 12 tones/sequence (ISI = 800ms)
- Standard stimulus: 1000 Hz tone
- Deviant stimulus: 1300 Hz tone (overall probability of a deviant = 12.5%)
- Each sequence contained 0, 1, 2, or 3 deviant tones
- Part I – Subjects ignored tones
 - Subjects pressed a button at the onset of each image acquisition (to monitor attention)
- Part II – Subjects attended to high-pitched tones
 - Subjects pressed 1 of 4 buttons at the onset of each image acquisition to indicate the number of high-pitched tones they heard
- EEG:
 - 64 channels
 - Band-limited from DC – 100 Hz and sampled at 500 Hz
- fMRI:
 - 1.5 T Scanner
 - T2*-weighted, gradient-echo, echoplanar images
 - TR = 12.25 sec (Acquisition time = 2 sec)
 - 21 contiguous axial slices (3.75 x 3.75 x 6 mm)

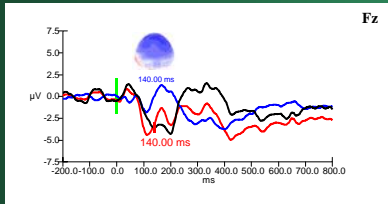
Design Advantages

- 1) Simultaneous EEG and fMRI
- 2) Clustered image acquisition
- 3) Elimination of activation caused by motor responses to targets and from extended cumulative counting of targets
- 4) Implementation of a new baseline condition
- 5) Whole brain imaging
- 6) Relatively large sample of subjects

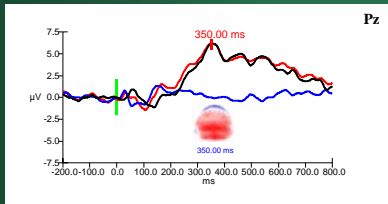
Results

Grand Average ERPs (Linked-Mastoid Reference)

Ignore Condition



Attend Condition

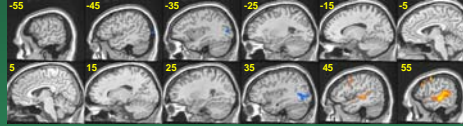


Standard
Deviant
Deviant – Standard

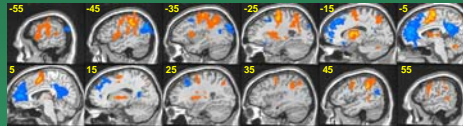
- A mismatch negativity (MMN) reflecting automatic auditory deviant detection and a P300 reflecting attentive auditory deviant detection were elicited in the Ignore and Attend conditions, respectively

Significant Areas of fMRI Activation

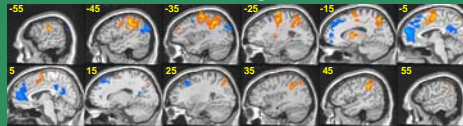
Deviant > Standard (Ignore Condition)



Deviant > Standard (Attend Condition)



Attend Condition > Ignore Condition



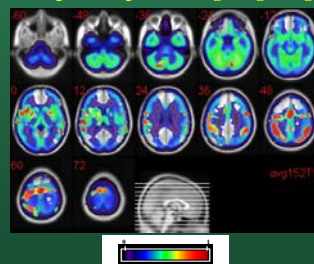
p < 0.005 (uncorrected)
p < 0.05 (corrected)

- Significant areas of fMRI activation included the right superior temporal gyrus in the Ignore condition and bilateral activation in the superior temporal gyrus, supramarginal gyrus, inferior and superior parietal lobules, medial frontal gyrus, precentral gyrus, anterior cingulate, thalamus, and putamen in the Attend condition
- Significant areas of fMRI deactivation included the left angular gyrus, left dorsal prefrontal cortex, left rostral cingulate sulcus, and bilateral deactivation in the posterior cingulate in the Attend condition

EEG Source Reconstructions

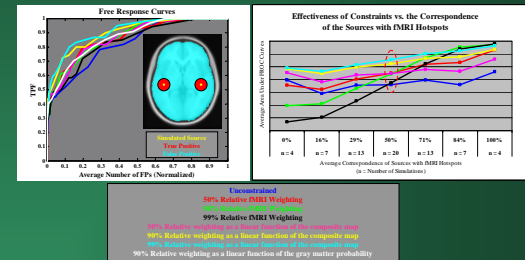
- The inverse problem is ill-posed, therefore additional constraints must be imposed in order to obtain a unique solution
- Minimum Norm Least Squares (MNLS) distributed source modeling with location-weighting was employed
- A 152-subject average T1-weighted image (MNI 152 brain) was used as the head model (standardized realistic Boundary Element Method (BEM) model)
- EEG source reconstructions were conducted using a 3-dimensional grid (5mm spacing)
- The effectiveness of various constraints (location-weighting schemes) on the inverse solutions was analyzed through the use of simulations
- Tested Location Weighting Schemes:
 - Unconstrained
 - Varying degrees of fMRI weighting
 - Varying degrees of composite weighting
- Composite Weighting: A location-weighting matrix consisting of anatomical, functional, and biophysical information to constrain the solution using relevant a priori information
 - Anatomical component
 - Gray matter probability
 - Functional component
 - Significant fMRI percent signal change (Activations and Deactivations)
 - Biophysical component
 - Gains at areas of significant fMRI activation

Example Composite Weighting Image



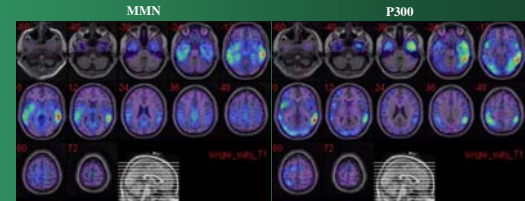
- Comparisons of the different location-weighting schemes were conducted using 20 "realistically" simulated data sets, with varying degrees of correspondence between the ERP sources and the fMRI activation foci
- The effectiveness of the different location-weighting schemes was determined using Receiver Operating Characteristics (ROC) methodology

Simulation Results



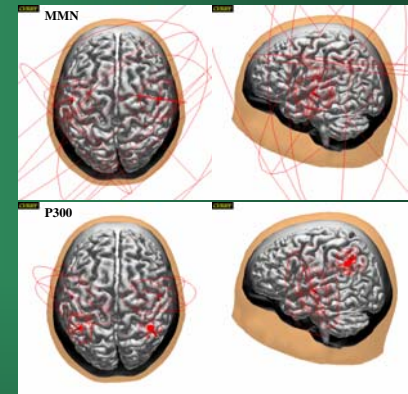
- The area under the individual ROC curves was used to test for differences in the effectiveness of the different location-weighting schemes
- It was found that 90% - 99% relative weighting as a linear function of the composite map was significantly more effective than all other constraints

Distributed Source Modeling



- Distributed source model using the empirically optimized location-weighting scheme at 140ms (MMN) and 350ms (P300)
- Areas of activation included the superior temporal gyrus which was lateralized to the right in both conditions and bilateral activation of the parietal lobe in the Attend condition

Spatio-Temporal Dipole Modeling



- Dipole model (based on the fMRI and distributed source modeling results) with corresponding confidence ellipsoids at 140ms (MMN) and 350ms (P300)
- Approximately 90% of the variance was explained by this model
- Bilateral activation of the superior temporal gyrus (right lateralized) during the occurrence of the MMN was followed by bilateral activation of the parietal lobe during the occurrence of the P300

Conclusions

- The main generators of the MMN were found in the superior temporal gyrus and were lateralized to the right
- The main generators of the P300 were found bilaterally in the posterior part of the superior temporal gyrus, supramarginal gyrus, and inferior and superior parietal lobules
- By more accurately determining the major neurophysiological origins of these ERP signals, it may be possible to expand the use of these components clinically

Acknowledgements

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