TIME IS OF THE ESSENCE

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INTRODUCTION

Temporal information is used for motion perception, sound localization, speech recognition, speech production, and motor tasks. Timing functions span modalities (e.g., visual, auditory, kinesthetic) as well as time scale (e.g., sound localization, perceptual timing and time estimation, etc). The notion that time is processed in a unitary central locus across scale and modality is in line with this perception, however, no single lesion abolishes temporal processing over all time scales. Here, we report differential activation within the visual system: millisecond timing activates visual areas, while the visual system is deactivated during second timing.

METHODS

Six subjects performed auditory temporal and frequency discrimination tasks during fMRI. There were two interval conditions. In the short interval condition, subjects decided whether comparison intervals were longer or shorter than a 100 ms standard interval. In the long interval condition, subjects decided whether comparison intervals were longer or shorter than a 1200 ms standard interval. In the frequency condition, subjects decided whether the pitch of comparison tones were higher or lower than 3.5 kHz. All tasks were adaptive, subject performance was held at about 80% to control for task difficulty.

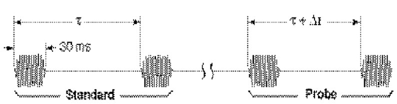

Figure 1: Auditory test stimuli. The interval variation, Δt, was adjusted adaptively such that the subjects were 75-80% accurate in determining whether the probe interval, τ+Δt, was longer or shorter than the standard interval, τ.

Scanning: All scanning was performed using a 3T Siemens Allegra scanner.

Event-related BOLD fMRI was performed using echo-planar scans (tr of 2.5, te of 50 ms, flip angle of 80°). Thirty axial slices, each 3mm thick were collected to provide whole-brain coverage.

Subjects were studied for three functional scans, one for each condition, where they were presented with 40 paired-tones. Stimulus presentation was jittered to allow estimation of the hemodynamic response. Standards were presented before the onset of MR Scanning.

A high resolution EPI localizer with identical readout bandwidth along the phase encoding direction(tr/te = 5000/33 ms, 128^2 matrix, 200 mm FoV, 3 mm slice with 1 mm gap, 2 shots/image and 4 NEX) and a high resolution structural scan utilized an MP-RAGE sequence (tr/te/ti 2300/2.1/1100 ms, 256^2 matrix, 256 mm FoV, 8° flip angle) were acquired.

Analysis: We analyzed our functional data using the FEAT (fMRI Expert Analysis Tool) within FSL.

Pre-processing: Preprocessing was standard. Slice timing correction, motion correction (MCFLIRT), brain extraction (BET), spatial smoothing (5 mm spatial convolution kernel) and both the image series and the model were high-pass filtered prior to contrast modeling. The data were also pre-whitened using FILM.

Contrasts and Models: A hemodynamic response model was created based on the convolution of the stimulus timing with an *a* priori model of the nominal hemodynamic "impulse" response. Each condition was contrasted with rest on a single subject level. After registration, the data were processed for second level (group effects) analysis using FSL's FLAME tool. Contrasts were all performed on the whole brain. We contrasted Short (Perceptual) and Long (Time Estimation) intervals with each other and with the control frequency discrimination condition. The FLAME analyses were thresholded using clusters determined by Z>1.5 (uncorrected)

RESULTS

Perceptual Timing: Acoustically-presented stimuli resulted in significant activations in both motor and visual brain areas (Figure 2A)

Visual Areas: The calcarine cortex, pontine nuclei, lingual gyrus including area 17, and the left pulvinar were significantly active when contrasted with frequency.

Motor Areas: The precentral gyrus, supplementary motor area (SMA/ pre-SMA)), basal ganglia (caudate, globus pallidus, red nucleus and cerebellum were significantly active when contrasted with frequency.

Other: The postcentral gyrus, dorsal lateral prefrontal cortex (DLPFC), L superior temporal gyrus,anterior and mid cingulate gyri were significantly active when contrasted with frequency. The left amygdala was deactivated when contrasted with frequency.

Perceptual Timing vs.Time Estimation: There is a substantial substantial differences in the regional recruitment for these two conditions. (Figure 2C)

Long > Short: The DLPFC, inferior frontal gyrus (more so on the right), amygdala, pre-SMA and R supramarginal gyrus were more active in time estimation than perceptual timing.

Short > Long: The precuneus, superior temporal gyrus, left posterior inferior frontal gyrus, cerebellar culmen/ pyramis, and parahippocampal gyrus were more active during perceptual timing than time estimation.

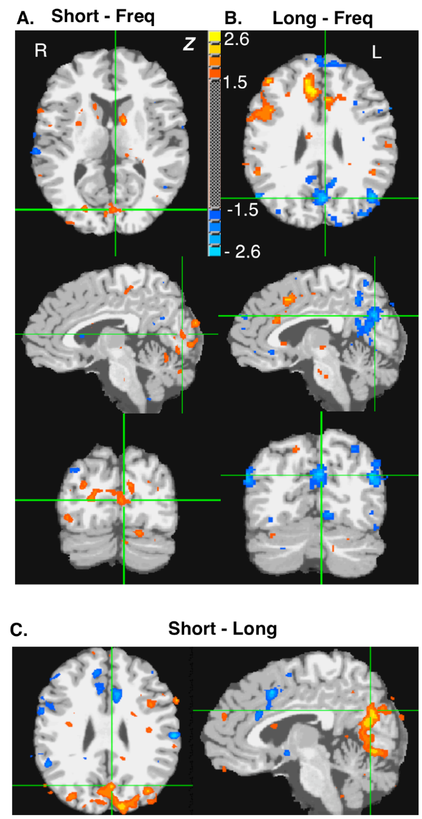

Figure 2: Comparison of visual regions in 100 ms and 1200 ms interval conditions. All contrasts thresholded for z values of magnitude greater than 1.5. **A)** Regions whose MR signal differed in the 100 ms interval discrimination compared to frequency include cuneus, precuneus, inferior, middle and superior occipital gyri. **B)** Regions whose MR signal was *reduced* in the 1200 ms interval discrimination compared to frequency included in the cuneus, precuneus, middle and superior occipital gyri **C)** Regions whose MR signal differed in the 100 ms interval discrimination compared to 1200 ms interval discrimination.

CONCLUSION

Interval discrimination in the millisecond range and second range utilize different neural circuits. Millisecond interval discrimination in the auditory modality activates classic visual areas, while second timing deactivates visual areas, consistent with a attention shift away from visual processes. Second interval discrimination, a more conscious process, relies more on frontal cortex than does millisecond timing.

Acknowledgements: This work could not have been done without the support of the Brain Mapping Medical Research Organization