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## Background

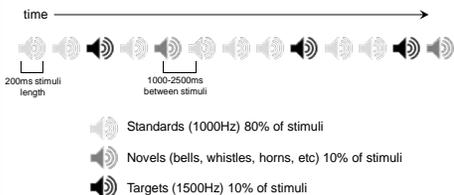
Pupillary dilatation has been used as a robust measure of cognitive processes, and the associated neural pathways are well understood (Cacioppo 2000). However, few studies have identified cortical brain regions that activate concomitant with dilatation. Also, previous pupil studies have examined many types of cognitive processes, but none have experimented with an oddball paradigm. We used a new method of fusing fMRI and pupil response data to identify joint spatially independent brain areas and temporally independent pupil responses that vary in the same linear manner as the pupil response during an auditory oddball task (Calhoun 2006).

## Hypothesis

We hypothesize that the pupil response would be greatest for target tones, lesser for novel tones, with nearly no response for standard tones. We expect the correlation analysis to show some similar areas found in the group average of the oddball task. Fusion ICA should produce one component for targets and one for novels. We also expect the fusion analysis to show areas of midbrain activating concomitant to the pupil dilatation.

## Auditory Oddball Task

Two runs of six minutes, thirty eight seconds each were completed during an fMRI session. Pupil dilatation was recorded concurrently at 240Hz, with an accuracy of 0.1mm.



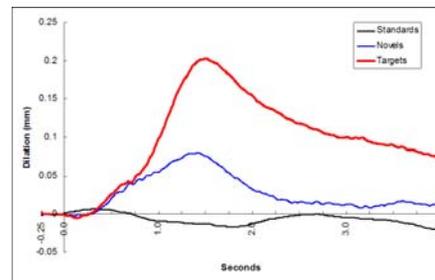
## Methods

We tested 19 healthy control subjects (ages 18-49, 37% male) using BOLD fMRI (TR=1500ms) in a Siemens Allegra 3T magnet while simultaneously collecting pupillary data using an ASL model 5000 eye-tracker. Subjects performed an auditory oddball task consisting of 10% target, 10% novel, and 80% standard tones (Kiehl 2003). They pressed a button to respond only to target tones. fMRI data were realigned, normalized, smoothed, and statistics generated using the general linear model. Pupil response data were processed by removing blinks, and averaging the time courses surrounding the button presses. The fMRI and pupil data for all subjects were entered into the Fusion ICA Toolbox (FIT, Calhoun et al), and statistics generated for the correctly identified target condition.

fMRI data were realigned using INRIalign, normalized to the standard EPI template, and smoothed at 4mm. Statistics were created using the general linear model (GLM) in SPM2, generating first level (subject) and second level (group comparison) statistics.

## Pupil Dilation Results

Pupil response averages showed dilatation of 0.203mm (+/- 0.108mm) for targets, 0.08mm for novels, and 0.006 for standards. Peak response for targets occurred at 1.503 seconds.

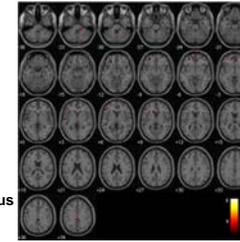


## Correlation Results

Several areas of interest were found in correlation analyses, all positive ( $p < 0.001$ )

### Targets with peak pupil dilation:

- L cingulate gyrus**  
(-3,-33,39)  
(Brodmann 31) [t=3.72]
- L inferior frontal gyrus**  
(-51,39,6)  
(Brodmann 45) [t=4.21]
- R medial frontal gyrus**  
(3,57,6)  
(Brodmann 10) [t=5.27]
- R pons**  
(18,-33,-33) [t=4.36]
- R superior temporal gyrus**  
(51,-15,0) [t=4.47]

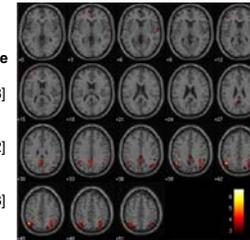


### Novels with peak pupil dilation:

- L medial frontal gyrus (Brodmann 8) [t=4.08]

### Targets with latency of peak dilation:

- L precuneus**  
(-3,-66,33)  
(Brodmann 7) [t=4.27]
- L inferior parietal lobule**  
(-51,-60,48)  
(Brodmann 40) [t=6.18]
- L medial frontal gyrus**  
(-3,60,3)  
(Brodmann 10) [t=4.32]
- L inferior frontal gyrus**  
(-51,39,15)  
(Brodmann 46) [t=5.73]



### Novels with latency of peak dilation:

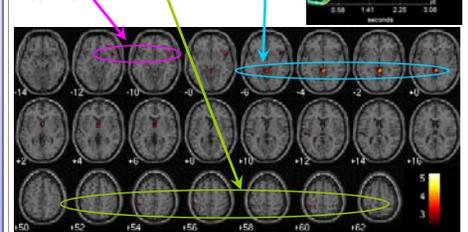
- R precuneus (Brodmann 19) [t=3.84]
- R superior parietal lobule (Brodmann 7) [t=4.88]

## Fusion Results

Fusion analysis produced one component for target tones and one for novels. The following areas were of particular interest.

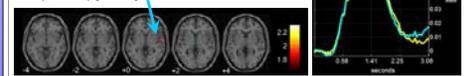
### Fusion for targets ( $p < 0.001$ )

- L Inferior Parietal Lobule**  
(Brodmann 40)  
(-42,-42,60) [t=3.95]
- Sup. Temporal Gyrus**  
(Brodmann 38) (54,15,-12) [t=4.58]
- Culmen** (3,-45,6) [t=3.88]
- Midbrain** (6,-36,-3) [t=3.45]



### Fusion for novels ( $p < 0.05$ )

- Superior Temporal Gyrus**  
(Brodmann 22)  
(63,-6,-3) [t=2.30]



## Conclusions

As anticipated, pupil response was largest for target tones, smaller for novel tones, and there was almost no response for standard tones, suggesting greater involvement of autonomic systems with increased attention and cognitive demands for targets and novels.

Correlation analysis identified a subset of regions previously found to be engaged by target and novel stimuli, suggesting that activity in these areas may contribute to mediating the pupil response.

ICA fusion found one fMRI component that matched pupil response for targets and another for novels. Brainstem and cerebellar engagement was expected as these regions logically could plan a role in coordinating relatively involuntary muscular aspects of the pupil response. However, both correlation and ICA found evidence for cortical engagement in this response, with novels predominantly engaging more posterior brain regions. Future research will help to better determine the nature of these associations.

## References

- Kiehl, K. A. and P. F. Liddle (2003). "Reproducibility of the hemodynamic response to auditory oddball stimuli: a six-week test-retest study." *Hum Brain Mapp* 18(1): 42-52.
- Calhoun, V. D., T. Adali, et al. (2006). "Neuronal chronometry of target detection: fusion of hemodynamic and event-related potential data." *Neuroimage* 30(2): 544-53.
- Cacioppo, J. T., L. G. Tassinary, et al. (2000). *Handbook of psychophysiology*. Cambridge, UK ; New York, NY, USA, Cambridge University Press.