Activation of the Inferior Olive

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Introduction

The inferior olive (IO) is a group of nuclei in the brainstem and is the sole origin of climbing fibers to the cerebellar cortex. While complete functions of the IO are unknown, it is believed to contribute to temporal processing. Functional magnetic resonance imaging (fMRI) studies have shown activation of the inferior olive by unexpected sensory stimuli. In this study, we tested the IO's sensitivity to stimulus timing change to determine the time-change that is most efficient in activating the IO in the hopes of being able to achieve reliable and robust activation of the inferior olive in humans to study diseases in which the IO is implicated.

Materials and Methods

Subjects were scanned while observing randomly presented anisochronous and isochronous sequences. They were instructed to indicate whether the sequence was isochronous or anisochronous by pressing one of two buttons in a forced choice fashion. Each anisochronous sequence consisted of 7 visual stimuli occurring at 1 Hz with the exception of one deviant stimulus that was presented prematurely by 50, 100, 200, 300, 400, 500, 700, and 800 ms. The deviant stimulus was presented pseudo-randomly as the 4th, 5th or 6th stimulus within the anisochronous sequence. Thus, at least 3 stimuli (2 inter-stimulus intervals) occurring at 1 Hz will precede the deviant stimulus to establish isochronicity allowing the subjects to recognize the change in timing of the deviant stimulus. An ISI that is shorter than the regular ISI (of 1000 ms) was used to avoid accounting for a neural response to what might be perceived as an "omitted" stimulus if the deviant stimuli were to be presented after the expected regular stimulus time.

Each "true" isochronous sequence consisted of 7 stimuli occurring at 1 Hz (with no deviant stimulus). True isochronous sequences were presented to monitor subjects' performance and were not used in further analysis. Subjects who perform poorly in trials with true isochronous sequences were excluded. The ratio of true isochronous sequences to anisochronous sequences was 3:1. However, subjects were not aware of this ratio.

Figure 1: *Activation from all of the timing changes (50-800 ms)*

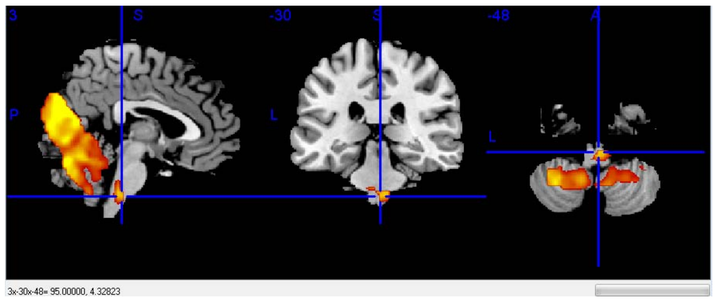


Figure 2: *Activation from the 300 ms timing change*

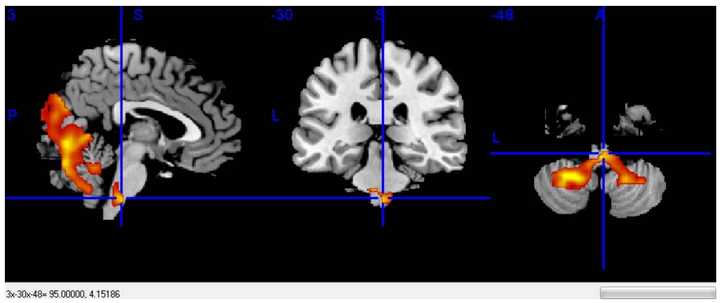
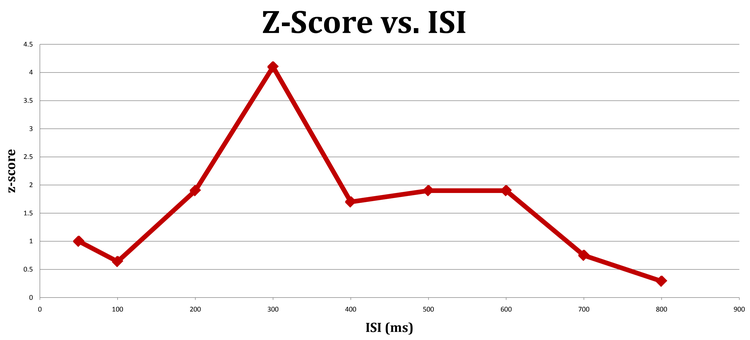


Figure 3: *Z-score for the activation of each of the timing changes*



Results

When group all the timing changes from 50 to 800 ms, there is strong IO activations (see Figure 1). For single timing change, there is a strong IO activation at 300 ms (Figure 2). The z-score was highest for the 300 ms ISI; all are shown in Figure 3. For 200ms, 400ms and 600ms, the IO activation reaches 0.05 after small volume correction. For 500 ms and 700ms, the IO activation reaches 0.05 without small volume correction. Generally, the data indicate that the IO is activated by timing changes from 200 to 600 ms.

Conclusions

- It has been shown that the inferior olive is activated by timing changes of 50 to 800 ms, confirming our hypothesis.
- The 300 ms change produced the largest effect.
- Strong inferior olive activation can be produced consistently in a controlled environment, enabling us to further explore diseases in which the IO is the involved.

References

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