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The effect of stimulus predictability on cerebro-cerebellar verbal working memory processing: An fMRI study

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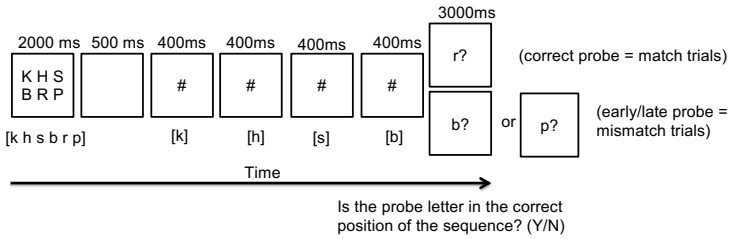
Introduction

- Making predictions about the future states of the body or the environment is crucial for efficient and adaptive goal-directed behavior.
- In the motor domain, the cerebellum is thought to play a key role in movement control by predicting the consequences of one's own actions through an internal forward model. An error signal is generated if there is a discrepancy between the predicted and the actual sensory feedback (Wolpert et al, 1998).
- In a previous transcranial magnetic stimulation (TMS) study (Sheu et al., 2019), we demonstrated that a similar predictive process can be extended to verbal working memory. Specifically, we found participants' ability to correctly predict the next letter in the sequence was impaired followed by cerebellar TMS during rehearsal.
- In the currently study, we used functional neuroimaging and a guided rehearsal verbal working memory task to examine how the cerebro-cerebellar network responded when a probe letter appeared in its predicted position within a sequence (correct probe = match) and when a probe letter was either one letter earlier (early probe = mismatch) or later (late probe = mismatch) in the sequence.

Methods

Participants: 19 (7 males), right-handed, healthy adults between 19 and 30 years old, participated the study. All were native English speakers.

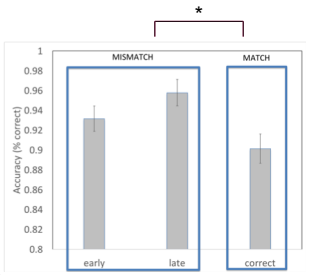
Guided Rehearsal Verbal Working Memory Task: During fMRI scanning, participants were asked to encode a 6-letter sequence, and to covertly rehearse these letters in sync with the guided symbol # on the screen. Because the rehearsal was guided, participants could easily predict the identity of the next correct letter in the sequence. When a probe letter appeared, the participant pressed button 1 to indicate that it matched the letter in the sequence, or button 2 to indicate that it did not match. The experiment consisted of 80 trials (40 correct probe match trials, 20 early probe and 20 late probe mismatch trials) with the probe appearing at the 5th position. An additional 16 trials with the probe appearing either at 3th or 4th position were added to ensure that the timing of the probe was unpredictable.

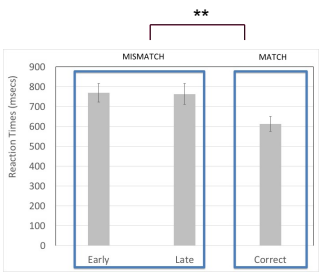


Scanning Parameters: 3T Philips Achieva scanner, T2*-weighted EPI (44 axial slices, TR/TE= 2300/30 msec, flip angle = 61°, 2.5 x 2.5 x 3 mm^3 voxel size).

fMRI Analysis: Pre-processing steps were performed with SPM12, including slice timing and motion correction, co-registration, segmented normalization, and smoothing at 6 mm FWHM. Physiological noise correction of cardiac/respiratory phase was performed using PhysIO Toolbox. Regressors of interest included Phase (Encoding vs. Probe) and Probe Type (Early/Correct/Late). Since no difference was found between Early and Late Probe, we lumped them together as a single "Mismatch" condition.

Behavioral Results



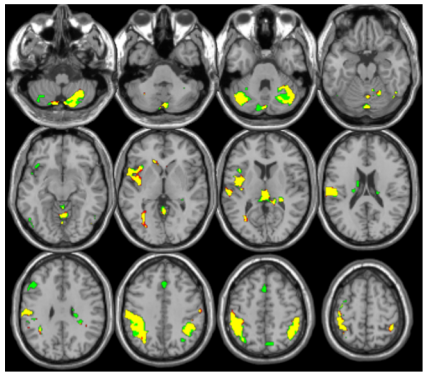


Participants responded significantly faster (~133 msec) to the probe letter when the probe appeared as a match (i.e. predicted stimulus) compared to a mismatch (i.e. unpredicted stimulus). However, the participants' performance were less accurate in match trials, suggesting there might be a slight trade-off for processing speed than accuracy for correct probe (match trials).

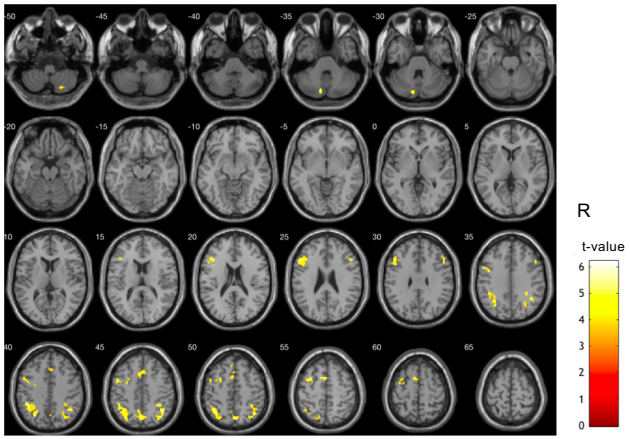
* p<0.05
** p<0.001

Imaging Results

Overlap (yellow) between Match (Red) & Mismatch (Green)



Mismatch (Early + Late probe) **> Match** (Correct probe)



Both the match and mismatch trails activated a similar fronto-parietal-cerebellar network typically found during working memory tasks (left figure). However, significantly less activity was found in this fronto-parietal-cerebellar network for the match trials compared to the mismatch trials (right figure). $P_{FWE\text{-}corrected}<0.05$, height threshold t = 3.61, k = 67 voxels.

Conclusion

- Our results suggest that the human brain spontaneously anticipates forthcoming sensory stimulus which allows predicted stimuli (matches) to be processed faster and require less neural activation than the unpredicted stimuli (mismatches).
- The cerebellum could be the loci of internal "forward" models which not only generates predictions of upcoming actions for motor control, but also generates predictions of the content in the phonological store to facilitate verbal working memory processing.

References

Wolpert, D.M., Miall, R.C., and Kawato, M. (1998). Internal models in the cerebellum. Trends Cogn Sci 2(9), 338-347.

Sheu, Y.S., Yu, Liang, Desmond, J.E. (2019). Disruption of cerebellar prediction in verbal working memory. Front. Hum. Neurosci. 13, 61.

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