Increases in cerebro-cerebellar activation with increasing memory load and task practice: An fMRI study

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Introduction: Verbal working memory (VWM) relies on a phonological store that must be periodically refreshed by articulatory rehearsal - the so-called phonological loop. Neuroimaging studies have postulated specific cerebro-cerebellar pathways underlying efficient VWM performance[1]. Behavioral VWM experiments show a linear increase in reaction time (RT) as the number of items in memory increase[2]. Previous investigations of VWM have demonstrated monotonic increases in activation of dorsal lateral pre-frontal cortex and Broca's area with increasing memory load[3]. This linear increase in activation during VWM has not yet been addressed in the cerebellum. Additionally, a consensus has not been reached as to the underlying neural mechanisms responsible for changes in neural activation with increased task practice, although theories based on increased neural efficiency[4] and functional neuroanatomical re-organization[5] have been proposed. The present study investigates the functional activation of the cerebro-cerebellar circuitry with increasing memory load and task practice. We hypothesize that increases in RT and task proficiency will be linearly related to increases in brain activation.

Methods: Sixteen right-handed participants (7 male, 9 female) were imaged within a 3.0T GE Signa scanner while performing a block design VWM task. They remembered 2, 3, 4 or 6 letters (list length) presented sequentially at 1 item per second, sub-vocally rehearsed these items during a 5 second retention interval, and subsequently identified whether a probe/lure item was included in the studied set. Both accuracy and response latency were measured. Each subject completed 3 sessions of 48 trials. A gradient echo spiral pulse sequence (TR = 2000 ms, TE = 30 ms, flip = 75 deg) was used. Whole brain functional scans (32 slices) were collected in the coronal plane with an inplane resolution of 3.75 mm and 6 mm slice thickness.

Results: Both reaction time (Fig. 1A) and brain activation (Fig. 1B) showed significant linear increases with increasing memory load. There was an overall significant increase in RT with increasing memory load ($F(3,45)=26.95$, $p<.001$) and a significant decrease with increased task practice ($F(2,30)=3.35$, $p<.05$). The load x practice interaction was not significant. The RT increase as a function of memory load had a significant linear ($F(1,15)=62.95$, $p<.001$), but not quadratic trend. Brain activations indicated linear load responses in left precentral (BA 6), inferior frontal (BA 47), parahippocampus (BA 35/36), inferior parietal (BA 40), superior cerebellum (VI/Crus I), and right inferior frontal (BA 47/46), superior (VI/Crus I) and inferior (VIIIA/VIIB) cerebellum. Quadratic trends were evident in left inferior parietal (BA 40) cortex and both linear and quadratic trends were found in left inferior parietal (BA 40), right inferior frontal (BA 47), right superior cerebellar (Crus I) and bilateral cingulate (BA 32) regions. *A priori* ROI analysis of specific sub-regions, as well as whole brain contrast maps, confirmed a significant increase in right inferior cerebellar and left inferior parietal activation from sessions 1 to 3 (Fig. 1C).

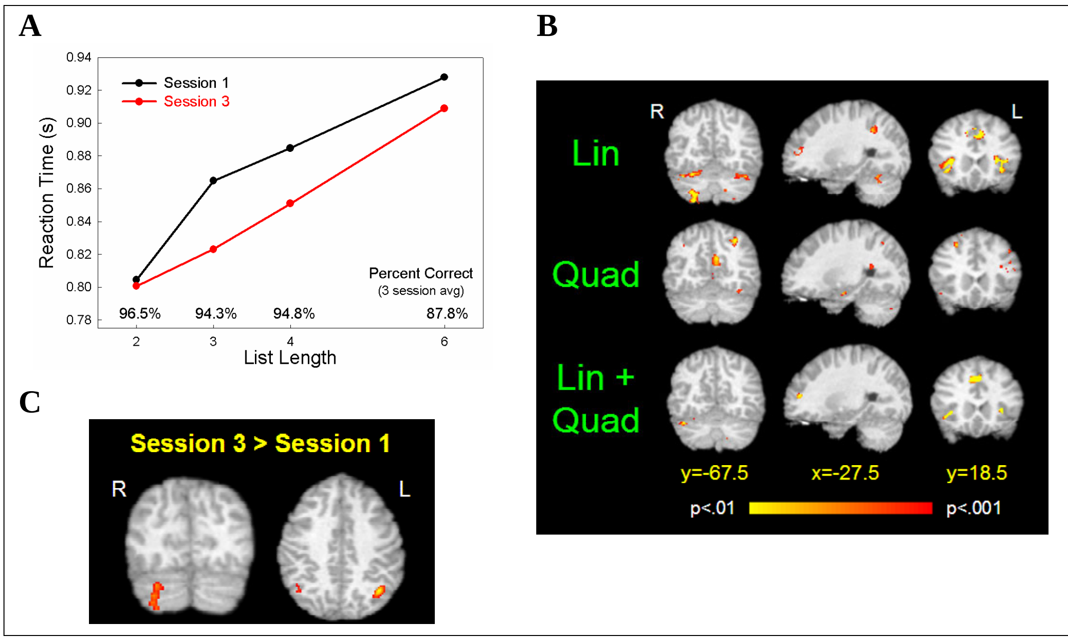

Figure 1

A. Plot of reaction time vs. memory load (list length) for sessions 1 and 3. Average accuracy for each list length is indicated at the bottom of the plot.

B. The 3 panels represent conjunction analyses at the p<.05 level, followed by thresholding between p<.01 and p<.001, to identify regions where linear alone, quadratic alone, and combined linear and quadratic trends are present.

C. Regions showing significantly increased activation in session 3 relative to session 1. Images thresholded at p<.005.

Discussion: Both reaction time and cerebro-cerebellar activations increased predominately linearly with VWM load. Purely quadratic increases were limited to the left inferior parietal region. Activations in left inferior parietal and right inferior cerebellum increased with improved task proficiency, suggesting that changes in this cerebro-cerebellar network underlie practice-related increases in efficiency of VWM performance. These results support and extend the current cerebro-cerebellar model of verbal working memory[3].

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