Valid fMRI timecourse analysis with tasks containing temporal dependencies

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.VALID fMRI TIMECOURSE ANALYSIS WITH TASKS CONTAINING TEMPORAL DEPENDENCIES

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Working memory paradigms contain temporal dependencies (e.g., the encoding period always precedes the delay period), which led Postle (2005) to hypothesise that the pattern of event-related fMRI timecourse activity reported by Slotnick (2005) may have been due to activity associated with preceding events. In the present analysis, both empirical and simulation results provide evidence that is inconsistent with Postle’s hypothesis and supports the extant interpretations of Slotnick.

The empirical analysis was limited to the superior frontal sulcus region—of-interest 1 cm anterior to the superior frontal sulcus/precentral sulcus junction (as this region is of greatest theoretical interest), and the amplitude of event-related timecourse activity was assessed 6 s following event onset (Slotnick, 2005). In this region, working memory delay related activity was significantly greater than zero [0.50 ± 0.10, mean ± one standard error % signal change, t(9) = 4.9, p < .01], saccade related activity was similar to zero [0.10 ± 0.05%, t(9) = 1.9, ns], and delay related activity was significantly greater than saccade related activity [0.60 ± 0.12%, t(9) = 4.8, p < .01] (Slotnick, 2005, Figure 4). It should be noted that this amplitude of working memory delay related prefrontal cortex activity (0.50%) is similar to that typically observed (and less than visual sensory related activity of ~1.0% amplitude). If Postle’s (2005) hypothesis is correct, the encoding period (always preceding delay) should be associated with significantly positive activity and the intertrial interval period (always preceding saccades) should be associated with little if any activity. Intertrial interval related activity was similar to zero [−0.13 ± 0.07%, t(9) = 1.9, ns]; however, encoding related activity was also similar to zero [0.10 ± 0.08%, t(9) = 1.3, ns]. (The identical pattern of results was obtained using the 4–8 s timepoints.) These results provide no evidence for encoding related activity, nor any differential activity that might confound the results of Slotnick (2005).

Based on the empirical evidence, the significantly positive activity observed in the superior frontal sulcus region (Slotnick, 2005) can be attributed to delay period activity (Figure 1a). Still, to further entertain Postle’s (2005) hypothesis (using the actual experimental protocol of Slotnick, 2005, rather than the alternative protocol considered by Postle, 2005), a simulation was undertaken assuming there was encoding (and no delay) related activity (with the same amplitude and standard error 6 s following onset as delay related activity; Figure 1b). Furthermore, following Postle (2005), it was assumed that baseline activity preceded encoding onset (Figure 1b, light grey area, mean baseline activity equals zero). Figure 1b shows that encoding related activity was similar to zero in the delay period [dark grey area, 0.07%, t(9) < 1, ns] and it was significantly less than the empirically
Figure 1. (a) Dashed and solid vertical lines demarcate the working memory encoding and delay periods, respectively. The haemodynamic response model of delay related activity (onset time = 7 s; see Slotnick, 2005, Figure 1) was scaled such that activity 6 s following delay period onset (dark grey area, time = 13 s) equalled the empirically observed mean delay period activity within the superior frontal sulcus (see text). (b) Haemodynamic response model of encoding related activity (onset time = 0 s), similarly scaled. Postle (2005) hypothesised that encoding related activity (with no delay related activity) could produce significantly positive activity in the delay period (dark grey area), and assumed the baseline preceded the encoding period (mean activity in light grey area equals zero). (c) Same model of encoding related activity with actual baseline used in Slotnick (2005), the 2 s preceding delay period onset (light grey area). The encoding related activity in the delay period (dark grey area) was always negative, ruling out the possibility that encoding related activity could produce significantly positive activity in the delay period.
observed value of 0.50% \( t(9) = 4.2, p < .01 \). In fact, only when the encoding activity peak amplitude was increased to 2.5%—far greater than even visual sensory related activity—did delay period activity approach 0.50% (a peak amplitude of 4.5% was required to reach 0.50%). The identical pattern of results was obtained when the encoding period included the initial instruction period (1 s preceding encoding), the pre-delay instruction period (1 s following encoding), or both.

It must also be clarified that the baseline assumed by Postle (2005) was not that used by Slotnick (2005). Rather, Slotnick defined baseline as the 2-s period preceding delay period onset. Figure 1c shows the effect of encoding related activity using the actual baseline employed (mean activity in light grey area equals zero). Encoding related activity was associated with significantly negative activity in the delay period [dark grey area, \(-0.42\%, t(9) = 4.1, p < .01\)], which was significantly less than the empirically observed value of 0.50% \( t(9) = 9.0, p < .001 \). Furthermore, as the amplitude of encoding related activity became more positive, the associated delay period activity became more negative (e.g., an encoding activity amplitude of 2.5% produced a delay period activity of \(-1.7\%\)). The identical pattern of results was obtained when the encoding period included either or both instruction periods.

Empirically, encoding related activity was shown to be similar to zero. Furthermore, simulations demonstrated that positive encoding related activity (had it existed) would have elicited negative delay period activity (using the actual baseline of Slotnick, 2005). These results are inconsistent with Postle's (2005) hypothesis that encoding related activity could have artifactually produced positive delay period activity. As such, the fMRI timecourse analysis results of Slotnick (2005) should be considered valid, and the differential working memory delay greater than saccade related activity in the superior frontal sulcus should be taken to reflect spatial working memory delay specific activity in the dorsal prefrontal cortex.

REFERENCES
