The contribution of the BOLD poststimulus undershoot to block-design subtraction outcomes in cognitive fMRI.

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INTRODUCTION: The poststimulus undershoot observed in event-related fMRI is generally considered unimportant in block-design studies, as it is thought to be small in comparison to the primary positive peak. A recent block-design fMRI study reported hippocampal deactivation in a transverse patterning task, which was specifically designed, on the basis of animal and human lesion literature, to engage hippocampal information processing. The current study employed a mixed block / event-related design in order to assess whether deactivation in the hippocampus was due to sustained changes on the block level, or to transient changes timelocked to stimulus presentation. Surprisingly, a very large hemodynamic undershoot was observed in the hippocampal-dependent "configural" condition compared to the control "elemental" condition, in the hippocampus and in other regions. Further analyses were conducted to evaluate the extent to which a greater poststimulus undershoot may cause outcomes of deactivation or non-activation in different brain regions, even in the presence of an enhanced positive peak of the BOLD response.

METHODS: Subjects (N=17) were presented with two pictures on a screen, and instructed to choose one with a button press. Auditory feedback indicated whether or not the choice was correct. In the configural condition (A>B, B>C, C>A), subjects were required to memorize the relationship between each pair of the three stimuli. In the elemental condition, (U>V,W>X, Y>Z), subjects only needed to remember the individual pictures as winning or losing. Subjects were pre-trained to high accuracy on both conditions before imaging. Stimuli were presented in blocks of 12, with a variable 3-7 sec. ISI, while whole-brain axial EPI images were acquired. A GLM analysis included a hemodynamically convolved boxcar state regressor reflecting sustained changes in the configural relative to the elemental condition, and 2 sets of finite-impulse response regressors for estimating the average hemodynamic timecourse in response to stimulus presentation in each condition.

RESULTS AND DISCUSSION: A standard block design analysis using only the boxcar regressor revealed positive activation in prefrontal and parietal regions, and deactivation in many standard "default-mode" regions, including bilateral hippocampus, medial prefrontal cortex, and posterior cingulate. When the FIR regressors were included, very little sustained activation was detected, suggesting that event-related transients account for the block-design results. Repeated measures ANOVA on the FIR timecourses revealed a condition X time interaction in several regions, which was always driven by the presence of both a larger positive peak and a larger negative undershoot in the configural condition. Random-effects analyses on the early and late timepoints, in conjunction with block-design results, revealed that positive activations were always driven by large positive peaks in the BOLD response (fig. 1A), whereas deactivations were driven by a larger undershoot (fig. 1B). In several areas, significant differences were seen in both early and late time ranges, but no activation was apparent on the block-design level, due to mutual cancellation of the signal differences in the two phases (fig. 1C). These findings suggest that the poststimulus undershoot may play a non-negligible role in determining the outcome of block-design fMRI experiments. We recommend that FIR models be used to evaluate the form of the hemodynamic response whenever possible, to disambiguate the effects of early and late differences of opposite sign.