ARTICLE IN PRESS

YNIMG-08775; No. of pages: 8; 4C: 4, 5, 6, 7

NeuroImage xxx (2011) xxx–xxx

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Review

The mixed block/event-related design

Steven E. Petersen [a,b,c,d], Joseph W. Dubis [a,*]

[a] Department of Neurology, Washington University School of Medicine, St. Louis, MO 63110, USA
[b] Department of Psychology, Washington University, St. Louis, MO 63110, USA
[c] Department of Radiology, Washington University School of Medicine, St. Louis, MO 63110, USA
[d] Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, MO 63110, USA

ARTICLE INFO

Article history:
Received 19 August 2011
Revised 27 September 2011
Accepted 28 September 2011
Available online xxxx

Keywords:
Mixed block/event-related
Transient
Sustained
Task control

ABSTRACT

Neuroimaging studies began using block design and event-related design experiments. While providing many insights into brain functions, these fMRI design types ignore components of the BOLD signal that can teach us additional elements. The development of the mixed block/event-related fMRI design allowed for a fuller characterization of nonlinear and time-sensitive neuronal responses: for example, the interaction between block and event related factors and the simultaneous extraction of transient activity related to trials and block transitions and sustained activity related to task-level processing. This review traces the origins of the mixed block/event-related design from conceptual precursors to a seminal paper and on to subsequent studies using the method. The review also comments on aspects of the experimental design that must be considered when attempting to use the mixed block/event-related design. When taking into account these considerations, the mixed block/event-related design allows fuller utilization of the BOLD signal allowing deeper interpretation of how regions of the brain function on multiple timescales.

Contents

Development of mixed design

Existing designs at time

With the advent of event-related designs, people's ambitions extended beyond just comparing different trial types using fMRI. Beginning in the late 1990s, researchers began using more complicated designs to look at multiple events within trials and to look at signals

* Corresponding author at: Department of Neurology, Washington University School of Medicine, Box 8111, 660 South Euclid Avenue, St. Louis, MO 63110.
E-mail address: JWDubis@npg.wustl.edu (J.W. Dubis).

1053-8119/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2011.09.084

that transcended single trials. It is because of this latter ambition that the mixed block/event-related design (hereinafter, the mixed design) was developed. This design was a combination of the two major extant designs—the block design and the event-related design. We will begin with sections related to each of these designs and their capabilities and then how the mixed design extends these capabilities.

Block design

In the early days, fMRI experimental designs mirrored those currently being used in experiments using PET—averaging the response of many closely spaced, successive trials over a short interval of time (i.e. 15–50 s). This initial experimental construct became known as block design. Block design experiments utilized blocks of either identical trial types to establish a task-specific condition or a mixture of trial types to establish a mixed task condition (Dale and Buckner, 1997). This experimental design conveyed a number of benefits that were useful for an emerging technique. First, block design experiments demonstrated efficiency by collapsing across many trials to attain an adequate signal-to-noise ratio (Bandettini, 1993; Dale and Buckner, 1997). Second, block design experiments are innately suited for detecting regions of interest (ROI) for particular tasks (Donaldson, 2004). Third, block design experiments are able to handle experimental tasks that do not fit into a trial-by-trial framework (i.e. continuous reading of a narrative or continuous finger-tapping task) (Maccotta et al., 2001; Meltzer et al., 2008; Ollinger et al., 2001b; Yarkoni et al., 2008).

Despite the benefits the design conveys, block design experiments are fundamentally limited. Most notably, the block design can not distinguish between trial types within a block (e.g., correct versus error trials), nor can they identify interesting within trial or across trial events (Buckner et al., 1996; Taylor et al., 2007). The block design does not account for the transient responses at the beginning and end of task blocks (Donaldson et al., 2001; Dosenbach et al., 2006; Fox et al., 2005; Konishi et al., 2001). Finally, in tasks where both positive and negative responses occur in a single block, the block design averages the two responses resulting in a canceling effect that does not represent the complexity and magnitude of the neural response (Meltzer et al., 2008).

Event-related design

With the insight that information about underlying neuron activity could be extracted from evoked hemodynamic responses, the urge to use more complex task paradigms resulted in efforts to improve the temporal resolution of fMRI analyses, leading to the development of the event-related design. This initial approach to event-related designs was inherited from ERP research (trial averaging) in electrophysiology. However, it was quickly realized that this averaging was not appropriate for hemodynamic responses to multiple trials (that could overlap in time). Thus, a formal convolution model of fMRI time-series was developed, in which the jittering of trials could be formulated in terms of design efficiency. Interestingly, the most efficient event-related design was in fact a block design. It was initially shown that averaging many similar trials–spaced so as to allow the hemodynamic response to resolve back to baseline prior to the next trial–could result in a trial-type specific timecourse (Boynton et al., 1996; Buckner et al., 1996). Follow-up work showed that inclusion of jittered fixation frames between trials allows for more closely spaced trials (Dale and Buckner, 1997; Miezin et al., 2000; Ollinger et al., 2001b). Trials of varying task-types could now be intermixed within a block while still being able to separate their timecourses.

The downside of the event-related design included a decrease of signal-to-noise leading to less power than block designs of similar timing (Miezin et al., 2000). Further, while the event-related design created a more fine-grained characterization of the BOLD activity, this methodology still ignored certain signals, including transients at the block transitions and sustained activity that begins and ends with the performance of the task. Consequently, the desire to take advantage of yet more unique signals in the BOLD response had not been realized.

Mixed block/event-related—dawning awareness

Our lab's first dawning awareness of the ability to overcome these issues was an important paper on top-down sustained effects during motion processing tasks (Chawla et al., 1999). In this paper, separate signals were described: a transient response related to the trials and a sustained response presumably related to top-down attention directed to MT from some sort of control system. An immediate concern when contemplating the sustained signal was that it was merely the result of misattributed transient activations. In the seminal paper, Chawla and colleagues showed the presence of sustained BOLD signal in V4, during a color task, and V5, during a motion task, even when no color or motion stimuli, respectively, were presented (1999). This evidence suggested that attending to and entering into a task mode, in the absence of ever performing the given task, is sufficient to elicit sustained BOLD signal.

This raised considerable excitement in our laboratory for several reasons. The most compelling was to address an issue raised conceptually by Tulving and empirically by the work of Düzel (1999). The issue was whether it was possible to distinguish adoption of a retrieval mode that goes across a period of task performance from a retrieval success effect that is determined on a trial-to-trial basis. In the Düzel work, event related potentials showed a constant electrophysiological signal that appeared to be related to the mode and trial-related activity related to success. Our first attempt to address this was in 2001 (Donaldson et al., 2001). After months of fumbling through analytical difficulties, we were able to show separate sustained activity related to task blocks, as well as common transient activity related to trials. Further, in an examination of the residual activity that was not modeled, it also appeared as if there were signals at block transitions. Each of these signals could be seen within the same voxel, as in the original Chawla paper. While we did not feel that the question of retrieval mode was answered in this paper, it strongly encouraged us to move more deeply into the use of this methodology.

The mixed design in Chawla et al. rests on modeling both block and event-related effects in the extracted BOLD activity. Chawla et al. were interested in the interaction between these two factors; namely the attentional (block factor) modulation of visual (event factor) responses. More generally, the modeling of both sustained and transient responses allows one, in principle, to separate set or mode-related neuronal activity from stimulus or task bound components. In the next section, we will examine the design itself, and then in the following sections, some of the uses it has been put to including memory and development.

Methodological considerations

Benefit

Identification of multiple temporal codings that suggest possibility/likelihood of ROIs performing separate/multiple processes that act over different timescales

At this point, in the early 2000s, the use of the mixed block/event-related fMRI design (Chawla et al., 1999; Donaldson et al., 2001) focused on the identification of separate trial-related activity and a sustained signal that persisted across an entire block. Fig. 1 demonstrates how the three fMRI design methods extract different signals from the BOLD activity. This distinction requires one to contemplate neural function associated with the modeled BOLD response differently than in both block designs and event-related designs as findings from mixed block/event-related designed studies suggest the

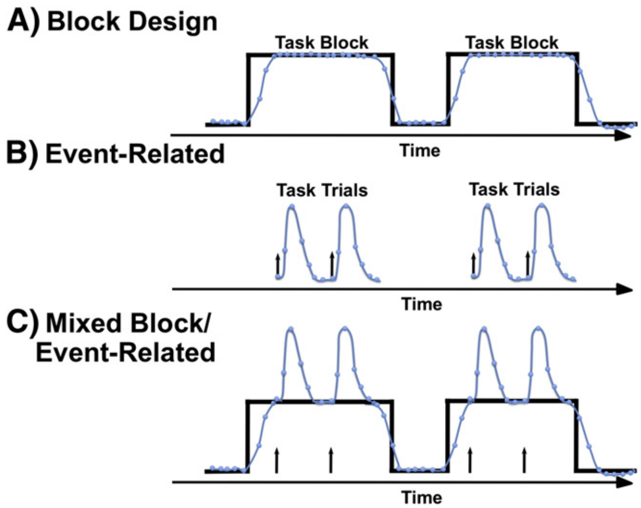


Fig. 1. Contrasting fMRI experimental designs allow for dissociation of different task-related signals. A) Block designs measure total neural activity across a task block to yield a single magnitude of activity that reflects both the sustained and all forms of transient BOLD activity. B) Event-related design utilizes jittered trials in order to model the transient responses of separate trial types. This model ignores the sustained BOLD activity and transient activity at block transitions. C) Mixed block/event-related designs allow for the simultaneous modeling of the transient, trial-related activity and the sustained, task-related BOLD activity.

possibility, perhaps even the likelihood, of ROIs concurrently performing multiple processes that act on different temporal scales.

Modeling of the transient, trial-related activity in the mixed design is identical to modeling event trials in an event-related design. Transient BOLD activity presumably reflects the neural response to processing of stimuli, computation of responses to stimuli, and the intermediate processes between these two more "peripheral" sets of processes.

The sustained signal is most often believed to represent a putative task maintenance signal (Donaldson et al., 2001; Dosenbach et al., 2006) perhaps related to task set (Sakai, 2008). Thus, regions showing sustained effects during encoding (Dennis et al., 2007; Otten et al., 2002), retrieval (Donaldson et al., 2001; Velanova et al., 2003), and object naming (Burgund et al., 2003) are active in an encoding-, retrieval-, and object naming-mode, respectively. This is not to be confused with regions and neural activity associated with encoding, retrieving, or naming of a specific stimulus.

As mentioned above, and as will be discussed more extensively below, there is a third type of signal that can be extracted using the mixed design. Transient BOLD responses that take place at task transitions (i.e. task onset and task offset) can also be modeled. Fig. 2 shows a schematic decomposition of the three task signals and how they may look in an actual BOLD timecourse. These signals may be related to instructional signals related to choosing to start a block, as well as more task-general control processes relating to the computation of task specific parameters, or state-switching signals (Dosenbach et al., 2006; Fox et al., 2005; Konishi et al., 2001).

Limitations

The mixed design is a very finicky beast in that poorly designed experiments do not just lead to a loss of power but to misattribution of signals from one type to the other. Further, the different signals, in practice, have very different power characteristics. As the mixed block/event-related design began to be used in labs across the field, considerations of the methodology were necessary to insure that the BOLD signal was accurately being parsed into its multiple separable components. Misattribution of BOLD signal across components can greatly affect one's results and conclusions.

Visscher et al. (2003) investigated instances of potential misattribution using both simulations and a test paradigm with counterphase checkerboard wedges in opposing hemifields. The wedges could be presented transient-only in one hemifield, sustained-only in one hemifield, or combined transient and sustained in a single hemifield. For the most part, relatively straightforward analyses of these responses to the stimuli reflected the fairly accurate way the signals or combination of signals were intended to produce. However, two situations occurred that showed how misattributions might take place.

The first was related to the visual simulation condition; the visual response to the sustained stimulus decreased over time. Fig. 3A depicts the modeled timecourse for the sustained stimulus decreasing over time. When only a sustained stimulus was presented, the analysis extracted a relatively accurate representation of the sustained activity. However, when a transient effect was modeled despite the lack of an evoking stimulus, the trial-related timecourse did not look like a normal hemodynamic response, but rather, it showed a continuously decreasing form. Fig. 3B depicts this decreasing, non-hemodynamically shaped transient timecourse. The presence of a modeled transient response when only a sustained stimulus was present suggested that BOLD activity from the sustained signal was being misapplied into the transient timecourse. Thus, the decreasing nature of the sustained activity "aliased" into a false trial-wise response. These transient effects are not stimulus-related in nature or appearance. In brief, the potential misapplication of BOLD signal between block and event related components make disambiguation a difficult feat that one must be particularly sensitive to in the statistical model. So, investigating the extracted timecourses in addition to the statistical maps can guard against conclusions of spurious transient effects.

Another situation where BOLD signal can be misapplied is when an assumed shape is used to model the transient events. Visscher et al. (2003) modeled simulated data with a SPM canonical waveform convolved with a boxcar of length 0.5–6 s. As the duration of the assumed hemodynamic response increased (broadening of the hemodynamic response relative to the original waveform), the correlation to the original waveform response decreased. This occurs because any deviation from the assumed shape gets aliased as (misapplied) sustained activity. Thus, assumed shapes should be used to model events in mixed block/event-related designs only with great care. This misapplication is more insidious than the first; inspection of timecourses will not alleviate the problem. Using a linear model with unassumed shape is preferred by our group (Miezin et al., 2000; Ollinger et al., 2001a,b).

Use of a mixed block/event-related design requires power considerations different from both block designs and event-related designs. As in block design experiments, mixed block/event-related design studies must alternate between blocks of baseline (for example fixation) and task blocks. Visscher et al. (2003) showed that a minimum of 77.5 s of total fixation (summed across all fixation periods) is preferred. This corresponds to 31 frames when the repetition time (TR) is 2.5 s. Below that threshold, the covariance, the amount that the estimate of one parameter is affected by the estimate of a second parameter, increases dramatically. Above that threshold, the benefit of additional fixation frames to reduce covariance is minimal as it does not appear to be a ratio of fixation frames to task block frames but rather the absolute number of fixation frames.

A second consideration is the number of frames in the modeled sustained response. Increasing the number of task frames in the modeled sustained response from 28 to 52 decreased the covariance (Visscher et al., 2003). An upper-bound on this limit has not been tested, though efficiency matters like scanner drift and subject fatigue need to be considered.

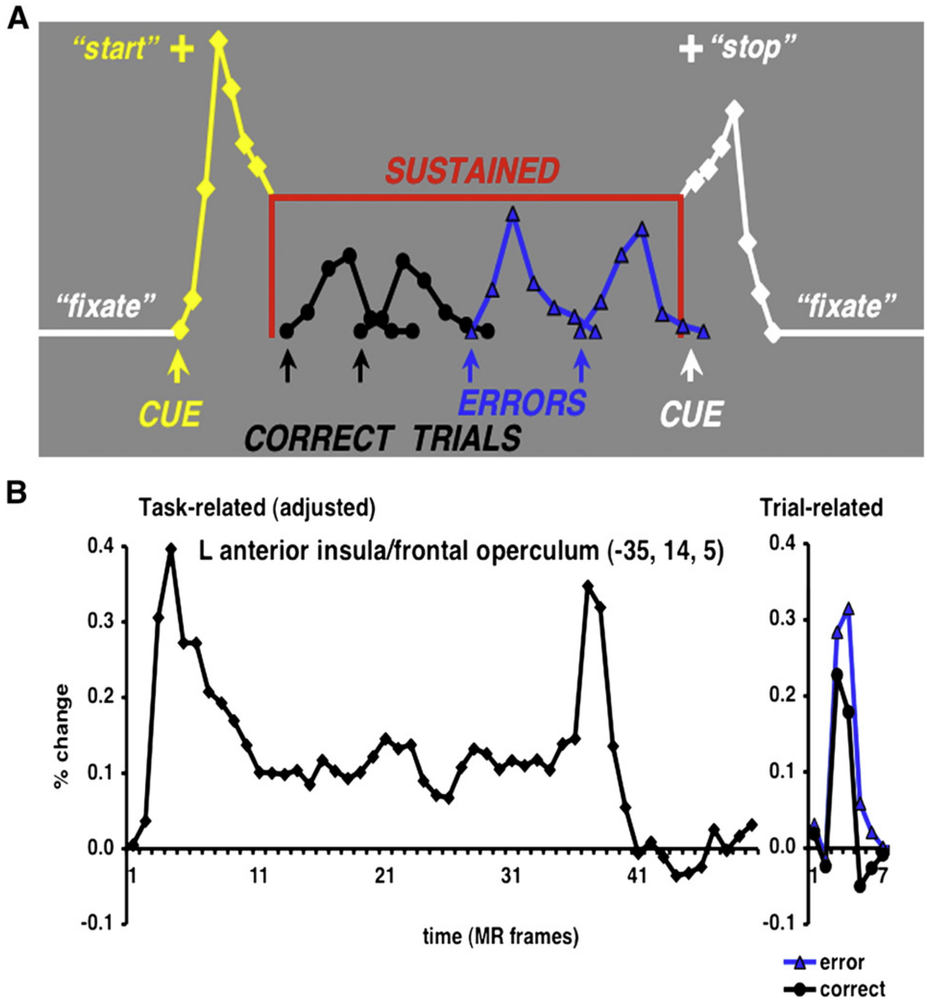


Fig. 2. Modeling task-related control signals in BOLD timecourses. A) The mixed block/event-related design allows for the simultaneous dissociation of three control signal. Transient activity at beginning of task (yellow) is believed to represent task initiation and implementation of task rules. Task set maintenance signals must be sustained (red) across the task block for continued performance. Performance correction comes from transient feedback responses (blue). B) The left set of timecourses reflect the residual activity after extracting the transient, trial-related activity from left anterior insula/frontal operculum showing block transition and sustained effects. Explicit modeling of these effects extracts their separate magnitude and reliability. Timecourse mirrors depiction of start-cue and sustained control signals from schematic in A. To the right are different trial-related signals related to error and correct trials, respectively. Figure previously published, reproduced with permission, in Dosenbach et al. (2006).

When designing mixed block/event-related design experiments, consideration of the number of subjects is necessary. Unlike the event-related trials where 10–30 trials can be included in a single block, only a single sustained estimation is extracted from each block (the same statement could be made regarding the task onset and offset responses though their empirical robustness makes the following a non-issue). Modeling the transient responses requires fewer subjects than modeling the sustained signal. Determining how many subjects are needed for an experiment is dependent on the type of response and the location of the response one is trying to model. For example, modeling sustained signals in the visual cortex at the within subject level (using fixed effects analyses) (Chawla et al., 1999) appears to be possible. However, at the between subject level (using random effects analyses) many more subjects may be required to adequately measure statistically significant sustained effects, especially in frontal cortex and parietal cortex (Dosenbach et al., 2006). A wide range of number of subjects (3 (Chawla et al., 1999); 9 (Donaldson et al., 2001); 34 (Velanova et al., 2003)) has been used in published studies using mixed block/event-related designs. While each experimental design is different relative to number of runs and number of blocks per type per run, our suggestion, based on our experience, is for 25–30 subjects. Below that, the statistical strength of the sustained signal is often poor.

A final consideration is the distribution of jitters. As in event-related designed experiments, mixed block/event-related designed experiments require the items (both block transitions and trials) to be jittered or spaced efficiently (Dale and Buckner, 1997; Friston et al., 1999; Miezin et al., 2000; Ollinger et al., 2001a; Ollinger et al., 2001b). However, unlike event-related designs, which often utilize an exponential distribution of jitters (Miezin et al., 2000), mixed block/event-related designs should consider utilizing a uniform distribution. This has two benefits: first, it elongates the task block by adding to the number of frames in the modeled sustained response, and second, it appears to allow a better separation and estimation of the transient responses.

Results of interest

The mixed design has been used in a large number of studies over the intervening years since its inception. We make no pretense here to have an exhaustive review of these studies. Rather, we will focus on two areas that seem to have utilized these designs: the search for memory modes and the development of sustained versus transient activity. A third highlighted set of studies, one in which we have toiled significantly, is the use of these different signal types to

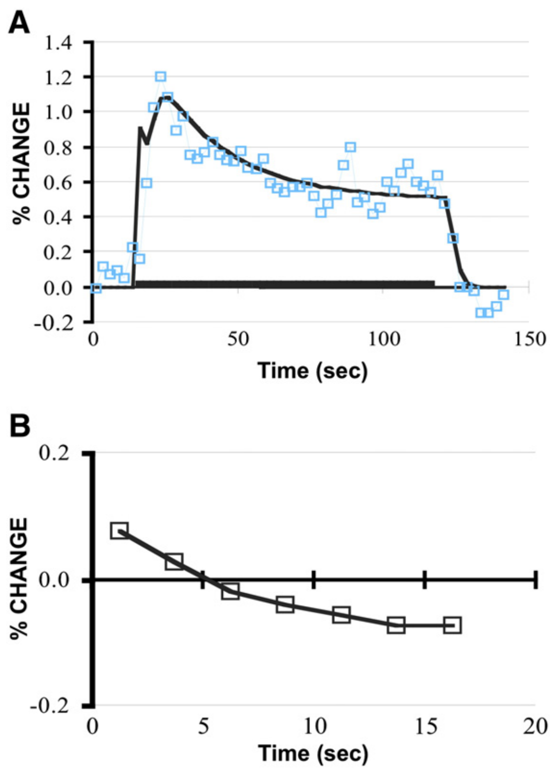


Fig. 3. Simulation of misapplied transient effects linked to decreasing sustained signal across time. Timecourse in A modeled for sustained effects only. Observation made that the sustained timecourse decreases across the task block. When the same data was modeled for both sustained and transient effects (B), in the absence of transient stimuli, a non-hemodynamic shaped transient response was extracted which corresponded to the decrease of sustained across time indicating a misapplication of sustained signal into the modeling of the transients. Figure previously published, reproduced with permission, in Visscher et al. (2003).

define control systems. The next three sections address each of these respectively.

Memory modes

Two papers published in 1998 (Brewer et al., 1998; Wagner et al., 1998), placed memory research at the focal point of trial-related activations reflecting behavior. Following this work, memory research soon expanded to determine if there were sustained activations that reflected entering into specific memory modes. For example, Fernandez et al. (1999) looked for an "encoding state". They reasoned that brain activity should reflect task performance on periods longer than individual trials but shorter than the experimental session. To test this, they had subjects memorize words in groups of five in a MRI scanner. Following a distraction interval, cued recall was conducted. By correlating the recall performance of a group words to the averaged neural activity across the encoding of the same five words, they concluded that the entorhinal cortex exhibited a slow modulation that was positively correlated with task performance. They proposed that this slow modulation, which they described as sustained, represented a declarative memory encoding state. At the same point in time, Düzel et al. (1999) were looking for a "retrieval state." They compared episodic retrieval (old/new) and semantic retrieval (living/nonliving) using a combination of PET and ERP. In both methods, they identified task-related but not trial-related differences between episodic-memory and semantic-memory retrieval. This work paralleled the concept of the mixed design but did not exactly use it.

Following Donaldson et al. (2001) use of the mixed block/event-related design to identify transient and sustained components of retrieval, others continued to utilize the design to study aspects of memory. Multiple groups (Dennis et al., 2007; Otten et al., 2002) utilized the subsequent memory paradigm to study encoding mode. While Otten and colleagues compared semantic and phonological judgments as implicit encoding methods, Dennis and colleagues investigated the effect of age on difference in memory (Dm). Little

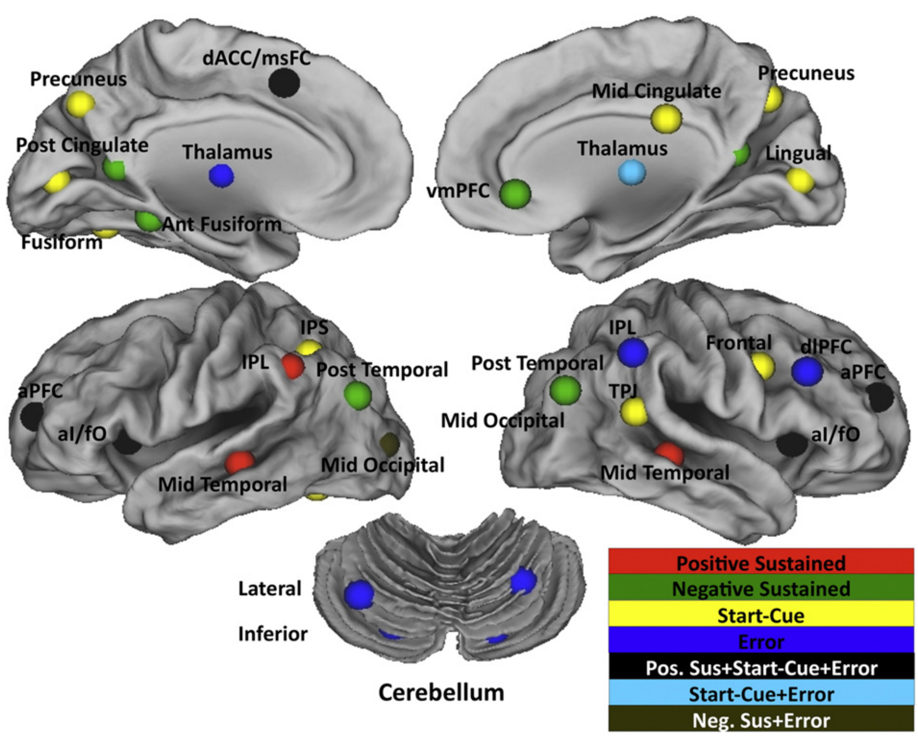
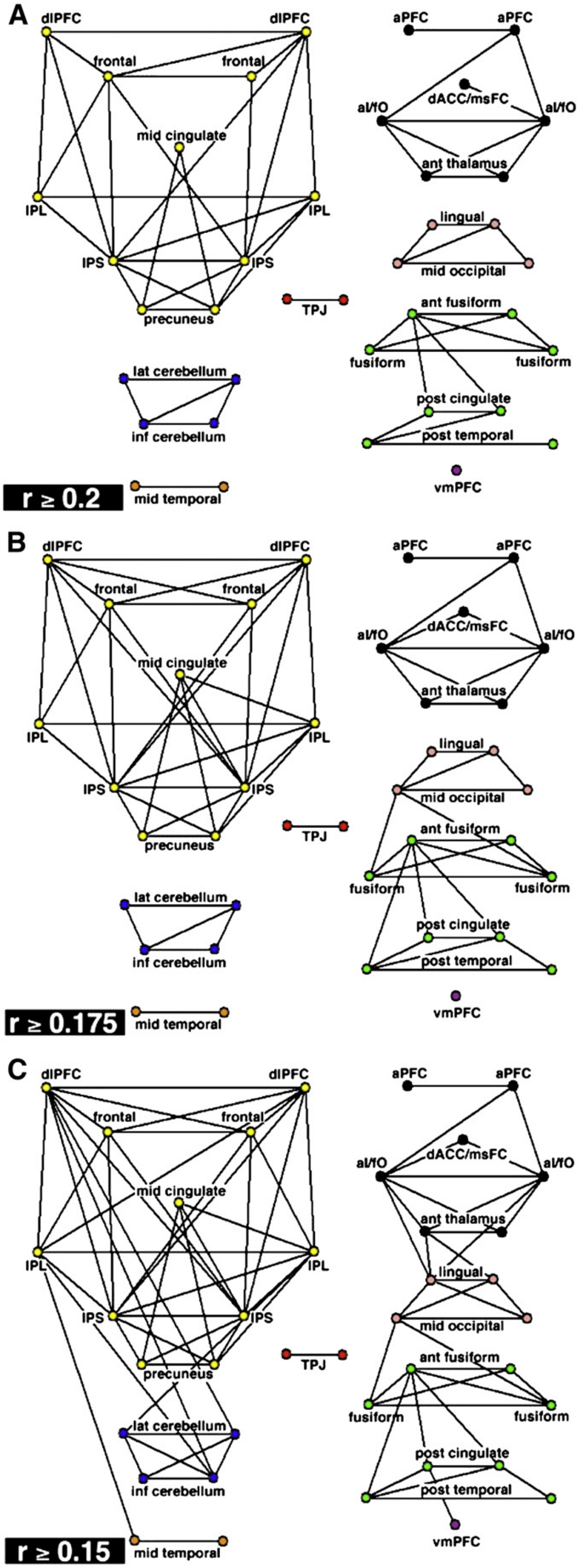


Fig. 4. Regions showing one or more putative control signal. Each of the three control signals (Start-Cue, Errors, Sustained (Positive and Negative)) were investigated to identify regions that were consistently robust to a given signal. Thirty-nine regions were identified. They are plotted according to control signal patterns listed in Dosenbach et al., 2007.



overlap was seen in regions of interest between the two studies. For example, Otten and colleagues identified a region of medial parietal cortex (0, −54, 60, MNI) in phonological encoding. Dennis and colleagues found a similar region (Young: −11, −53, 55; Old: −11, −56, 59, Talairach) in both young and old subjects. However, Otten and colleagues reported decreased sustained activity correlated with increased retrieval success while Dennis and colleagues reported increased sustained activity correlated with increased retrieval success.

Others (Velanova et al., 2003) investigated aspects of retrieval mode. Velanova and colleagues designed an experiment to compare retrieval of words intentionally encoded over 2 days with retrieval of words implicitly encoded during a pleasantness judgment immediately prior to scanning. As with the encoding studies, there was a lack of retrieval-specific regions, though Velanova et al. offered the possibility of task-general activations that would be later explored in Dosenbach et al. (2006).

Lifespan development

The disambiguation of transient and sustained activations using the mixed block/event-related fMRI design also allowed researchers to investigate how cognitive processing across multiple timescales may develop and how the functional roles of specific regions might change across time (Wenger et al., 2004). Burgund et al. (2006) compared children (ages 7–8) to young adults performing a matching-by-name and matching-by-physical appearance task on letters. They identified several regions–right lateral inferior frontal gyrus (40, 21, −1), right postcentral (57, −14, 21), left putamen (−20, −1, -3), left parietal-occipital (−14, −65, 18), and left lingual (−9, −91, −10) (all region coordinates in Talairach and Tournoux (1988))–that showed decreases of sustained activity with age. Simultaneously, these regions also showed increases of transient activity suggesting a shift from sustained to transient activity with age.

Jimura and Braver (2010) replicated a previous study by Braver et al. (2003) showing sustained activation in the anterior prefrontal cortex in blocks where task-switching occurs but not in blocks where only a single task was performed. When comparing older and younger adults, older adults (age 65–87) showed decreases in sustained activity during task-switching blocks but increases in transient activity during switch trials suggesting a change in task strategy. This finding–decreased sustained activity, increased transient activity–mirrors the development finding of Burgund et al. (2006).

Brahmbhatt et al. (2010) added to the literature by showing a similar trend (decreased sustained activity, increased transient activity with age) in children (ages 9–13) and adults performing a simple 0-back task. However, when the task-load was increased to 2-back, the pattern was inverted so that adults had greater sustained activity and less transient activity than the children. This change brought about by increased working memory load suggests the trend may be susceptible to task parameters such as working memory load or task strategy. While more research is required in this arena, the limited number of studies has suggested a linear trend of decreasing sustained activity matched by increasing transient activity across age from childhood to young adulthood to older adulthood.

Church et al. (2009) took usage of mixed block/event-related designs for studying development to the next stage comparing both typical children to typical adults and to adolescents with and without

Fig. 5. Task-control components in psuedoanatomical representation in young adults. Graph analysis, using 256 frames (640 s) of resting-state data, on previously defined control regions, in pseudoanatomical arrangement yields two, distinct control networks that are consistent across thresholds. (A) Thresholded at $r \geq 0.2$ ($P < 1 \times 10^{-9}$; two-tailed; Bonferroni corrected; *t*-test). (B) Thresholded at $r \geq 0.175$ ($P < 1 \times 10^{-7}$; two-tailed; Bonferroni corrected; *t*-test). (C) Thresholded at $r \geq 0.15$ ($P < 5 \times 10^{-5}$; two-tailed; Bonferroni corrected; *t*-test). Figure previously published, reproduced with permission, in Dosenbach et al. (2007).

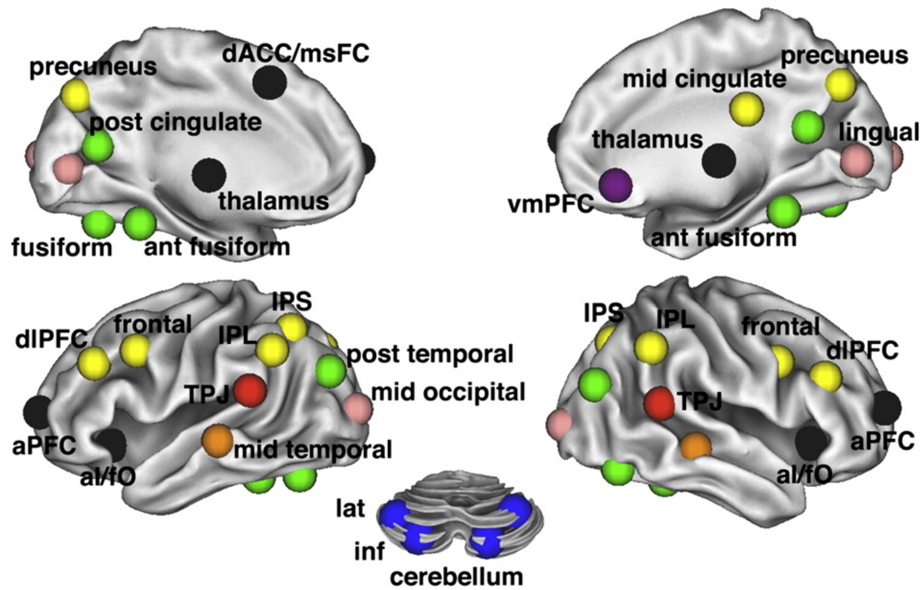


Fig. 6. Anatomical representation of task-control components. Eight separate components derived from the psuedoanatomical graph (r ≥ 0.2) seen in Fig. 5 and displayed on inflated surface rendering of the brain. Figure previously published, reproduced with permission, in Dosenbach et al. (2007).

Tourette Syndrome. By focusing on the start-cues and sustained activity, Church and colleagues were able to make observations about the development of task processes in individuals with Tourette Syndrome. They found that adolescents with Tourette Syndrome showed anomalous start-cue activity not seen over typical development, as well as increased sustained activity in frontal cortex, which is indicative of functional immaturity as this is also seen in younger typical children. This work serves as a blueprint for future investigations on the effects of neurological disorders on the development of task processing.

Control signals

The final set of studies we would like to address is from our own work. This set of studies is based on a search for regions that carry signals related to task level control. By task level control, we mean the set of control signals that tells other regions of the brain what to do in a particular test situation. So how might the signals look? Signals related to processing task instructions, orienting the subject toward a particular set of task demands, or used for instructing other regions about the kinds of things that must be done, would be instantiated as a transient signal at the beginning of a task block. Such block transition signals had been seen in an earlier work (Donaldson et al., 2001; Fox et al., 2005; Konishi et al., 2001), often not employing the mixed design per se, with various interpretations. A second form of signals, explicitly related to the mixed design, would be sustained activity across the performance of a task, putatively related to the maintenance of task parameters/top-down control signals. The third, less intuitive, set of signals would be related to performance feedback and could be operationalized as trial related signals showing systematic differences between correct and incorrect trials. Fig. 2 shows a schematic decomposition of the three task signals.

In a paper in 2006, Dosenbach et al. (2006; 2007) performed mixed design studies on 8 subject groups performing 10 different tasks searching for each of these three signal types. A large number of medial and lateral frontal and parietal regions showed some combination of the three signals, with several regions in the cerebellum showing only the error related feedback signals. Fig. 4 identifies regions identified in work by Dosenbach et al. (2006, 2007) consistently robust for one or more of the control signals. There was some systematicity in the signal combinations in that lateral and frontal parietal regions appeared to emphasize transient signals at the beginning of blocks, while medial frontal/anterior cingulate and anterior insular commonly showed sustained signals across blocks.

A subsequent study of resting state correlation between these regions further emphasized distinctions between them (Dosenbach et al., 2007). Lateral frontal and parietal regions correlated well with each other, cingulate and opercular regions correlated well with each other, but these sets did not correlate well at all with each other. These combined results strongly suggested that rather than a single control system, there are two separable control systems. Fig. 5 shows psuedoanatomical representations of distinct control networks across thresholds, and Fig. 6 shows corresponding anatomical placements. This evidence in total, and the arguments for this stance, are detailed in Dosenbach et al. (2008).

Conclusions

The mixed block/event-related design was developed to allow for simultaneous modeling of transient, trial-related and sustained, task-related BOLD signals. This advance from the block design and event-related design, respectively, resulted in researchers being able to look for BOLD signals related to task modes independent of the trials stimuli. While some areas of investigation (i.e. memory, development, and task control) have utilized the mixed design, its usage has not become widespread despite the potential benefits it conveys. The limitations and considerations of the design discussed here are indicative of the considerable care that must be given in its use, but when employed well, deeper attributions of function can be made then from either of the other more commonly employed designs.

Acknowledgements

Support for this research came from NIH grants NS37924 and NS06424, the McDonnell Foundation, and NIGMS grant T32 GM081739.

References

Bandettini, P.A., 1993. MRI studies of brain activation: dynamic characteristics. Functional MRI of the Brain. Society of Magnetic Resonance in Medicine, Berkeley.
Boynton, G.M., Engel, S.A., Glover, G.H., Heeger, D.J., 1996. Linear systems analysis of functional magnetic resonance imaging in human V1. J. Neurosci. 16, 4207–4221.

Please cite this article as: Petersen, S.E., Dubis, J.W., The mixed block/event-related design, NeuroImage (2011), doi:10.1016/j.neuroimage.2011.09.084

Brahmbhatt, S.B., White, D.A., Barch, D.M., 2010. Developmental differences in sustained and transient activity underlying working memory. Brain Res. 1354, 140–151.
Braver, T.S., Reynolds, J.R., Donaldson, D.I., 2003. Neural mechanisms of transient and sustained cognitive control during task switching. Neuron 39, 713–726.
Brewer, J.B., Zhao, Z., Desmond, D.E., Glover, G.H., Gabrieli, J.D.E., 1998. Making memories: brain activity that predicts how well visual experience will be remembered. Science 281, 1185–1187.
Buckner, R.L., Bandettini, P.A., O'Craven, K.M., Savoy, R.L., Petersen, S.E., Raichle, M.E., Rosen, B.R., 1996. Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging. Proc. Natl. Acad. Sci. 93, 14878–14883.
Burgund, E.D., Lugar, H.M., Miezin, F.M., Petersen, S.E., 2003. Sustained and transient activity during an object-naming task: a mixed blocked and event-related fMRI study. NeuroImage 19, 29–41.
Burgund, E.D., Lugar, H.M., Miezin, F.M., Schlaggar, B.L., Petersen, S.E., 2006. The development of sustained and transient neural activity. NeuroImage 29, 812–821.
Chawla, D., Rees, G., Friston, K.J., 1999. The physiological basis of attentional modulations in extrastriate visual areas. Nat. Neurosci. 2, 671–676.
Church, J.A., Wenger, K.K., Dosenbach, N.U., Miezin, F.M., Petersen, S.E., Schlaggar, B.L., 2009. Task control signals in pediatric Tourette syndrome show evidence of immature and anomalous functional activity. Front. Hum. Neurosci. 3.
Dale, A., Buckner, R., 1997. Selective averaging of rapidly presented individual trials. Hum. Brain Mapp. 5, 329–340.
Dennis, N.A., Daselaar, S., Cabeza, R., 2007. Effects of aging on transient and sustained successful memory encoding activity. Neurobiol. Aging 28, 1749–1758.
Donaldson, D., Petersen, S., Ollinger, J., Buckner, R., 2001. Dissociating state and item components of recognition memory using fmri. NeuroImage 13, 129–142.
Donaldson, D.I., 2004. Parsing brain activity with fMRI and mixed designs: what kind of a state is neuroimaging in? Trends Neurosci. 27, 442–444.
Dosenbach, N.U., Fair, D.A., Miezin, F.M., Cohen, A.L., Wenger, K.K., Dosenbach, R.A., Fox, M.D., Snyder, A.Z., Vincent, J.L., Raichle, M.E., Schlaggar, B.L., Petersen, S.E., 2007. Distinct brain networks for adaptive and stable task control in humans. Proc. Natl. Acad. Sci. U. S. A. 104, 11073–11078.
Dosenbach, N.U., Visscher, K.M., Palmer, E.D., Miezin, F.M., Wenger, K.K., Kang, H.C., Burgund, E.D., Grimes, A.L., Schlaggar, B.L., Petersen, S.E., 2006. A core system for the implementation of task sets. Neuron 50, 799–812.
Dosenbach, N.U.F., Fair, D.A., Cohen, A.L., Schlaggar, B.L., Petersen, S.E., 2008. A dual-networks architecture of top-down control. Trends Cogn. Sci. 12, 99–105.
Düzel, E., Cabeza, R., Picton, T.W., Yonelinas, A.P., Scheich, H., Heinze, H.J., Tulving, E., 1999. Task-related and item-related brain processes of memory retrieval. Proc. Natl. Acad. Sci. U. S. A. 96, 1794–1799.
Fernandez, G., Brewer, J.B., Zhao, Z., Glover, G.H., Gabrieli, J.D., 1999. Level of sustained entorhinal activity at study correlates with subsequent cued-recall performance: a functional magnetic resonance imaging study with high acquisition rate. Hippocampus 9, 35–44.
Fox, M.D., Snyder, A.Z., Barch, D.M., Gusnard, D.A., Raichle, M.E., 2005. Transient BOLD responses at block transitions. NeuroImage 28, 956–966.
Friston, K.J., Zarahn, E., Josephs, O., Henson, R.N., Dale, A.M., 1999. Stochastic designs in event-related fMRI. NeuroImage 10, 607–619.
Jimura, K., Braver, T.S., 2010. Age-related shifts in brain activity dynamics during task switching. Cereb. Cortex 20, 1420–1431.
Konishi, S., Donaldson, D., Buckner, R., 2001. Transient activation during block transition. NeuroImage 13, 364–374.
Maccotta, L., Zacks, J.M., Buckner, R.L., 2001. Rapid self-paced event-related functional MRI: feasibility and implications of stimulus- versus response-locked timing. NeuroImage 14, 1105–1121.
Meltzer, J.A., Negishi, M., Constable, R.T., 2008. Biphasic hemodynamic responses influence deactivation and may mask activation in block-design fMRI paradigms. Hum. Brain Mapp. 29, 385–399.
Miezin, F.M., Maccotta, L., Ollinger, J.M., Petersen, S.E., Buckner, R.L., 2000. Characterizing the hemodynamic response: effects of presentation rate, sampling procedure, and the possibility of ordering brain activity based on relative timing. NeuroImage 11, 735–759.
Ollinger, J.M., Corbetta, M., Shulman, G.L., 2001a. Separating processes within a trial in event-related functional MRI II. Analysis. NeuroImage 13, 218–229.
Ollinger, J.M., Shulman, G.L., Corbetta, M., 2001b. Separating processes within a trial in event-related functional MRI I. The method. NeuroImage 13, 210–217.
Otten, L.J., Henson, R.N., Rugg, M.D., 2002. State-related and item-related neural correlates of successful memory encoding. Nat. Neurosci. 5, 1339–1344.
Sakai, K., 2008. Task set and prefrontal cortex. Annu. Rev. Neurosci. 31, 219–245.
Talairach, J., Tournoux, P., 1988. Co-Planar Stereotaxic Atlas of the Human Brain. Thieme Medical Publishers, Inc., New York.
Taylor, S.F., Stern, E.R., Gehring, W.J., 2007. Neural systems for error monitoring: recent findings and theoretical perspectives. Neuroscientist 13, 160–172.
Velanova, K., Jacoby, L.L., Wheeler, M.E., McAvoy, M.P., Petersen, S.E., Buckner, R.L., 2003. Functional-anatomic correlates of sustained and transient processing components engaged during controlled retrieval. J. Neurosci. 23, 8460–8470.
Visscher, K.M., Miezin, F.M., Kelly, J.E., Buckner, R.L., Donaldson, D.I., McAvoy, M.P., Bhalodia, V.M., Petersen, S.E., 2003. Mixed blocked/event-related designs separate transient and sustained activity in fMRI. NeuroImage 19, 1694–1708.
Wagner, A.D., Schacter, D.L., Rotte, M., Koutstaal, W., Maril, A., Dale, A.M., Rosen, B.R., Buckner, R.L., 1998. Building memories: remembering and forgetting of verbal experiences as predicted by brain activity. Science 281, 1188–1191.
Wenger, K.K., Visscher, K.M., Miezin, F.M., Petersen, S.E., Schlaggar, B.L., 2004. Comparison of sustained and transient activity in children and adults using a mixed blocked/event-related fMRI design. NeuroImage 22, 975–985.
Yarkoni, T., Speer, N.K., Balota, D.A., McAvoy, M.P., Zacks, J.M., 2008. Pictures of a thousand words: investigating the neural mechanisms of reading with extremely rapid event-related fMRI. NeuroImage 42, 973–987.

Please cite this article as: Petersen, S.E., Dubis, J.W., The mixed block/event-related design, NeuroImage (2011), doi:10.1016/j.neuroimage.2011.09.084