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## **Single- and Multiple-Event Paradigms for Identification of Motor Cortex Activation**

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*AJNR Am J Neuroradiol* 2000, 21 (1) 94-98

<http://www.ajnr.org/content/21/1/94>

This information is current as  
of April 20, 2024.

## Single- and Multiple-Event Paradigms for Identification of Motor Cortex Activation

Michael Marquart, Rasmus Birn, and Victor Haughton

**BACKGROUND AND PURPOSE:** The “single-event” technique has been used as an alternative to the “block-trial” method to detect activation that may be accompanied by head motion. The purpose of this study was to compare the two methods for measuring activation in the sensorimotor cortex secondary to motor tasks.

**METHODS:** Functional MR imaging data were acquired from six participants as they performed tasks with their fingers, tongues, and toes in a block-trial and a single-event paradigm. For the block trial, the participant was instructed to perform the task when cued at a rapid self-timed rate for 15 seconds, alternating with 15 seconds of rest. Five periods of task performance and six rest periods were included in one acquisition. For the single-event method, the participant performed the task a single time every 15 seconds when cued by the investigator, for a total of 21 times. Using conventional parcellation methods, activation was detected by a cross-correlation technique and was classified as occurring in the sensorimotor cortex, supplementary motor area (SMA), or as nonspecific. Differences between the two acquisition paradigms were tested using the standard *t* test at a significance level of  $P < .05$ .

**RESULTS:** Activation was identified by both the block-trial and the single-event methods for the finger task, for the tongue task, and inconsistently for the toe task. More motion artifact occurred in conjunction with the toe and tongue tasks than with the finger tasks. On average, more activated pixels were identified by the single-event method than by the block-trial method. For these motor tasks, however, a larger percentage of pixels detected by the block-trial method than by the single-event method were specific for the sensorimotor cortex or SMA as sites of activation.

**CONCLUSION:** For the tongue and the toe movement tasks, which may produce some head motion artifacts, the single-event paradigm provides a useful alternative to the block-trial method for identifying the sensorimotor cortex or SMA. It does not achieve a greater percentage of activation within primary motor areas. For the finger movement task, which does not usually produce head motion artifacts, the block-trial method generally produced a greater percentage of activated pixels in the sensorimotor cortex or SMA than did the single-event method.

Functional MR imaging reveals areas of changing regional CBF (“activation”) resulting from neuronal activity. The resulting MR signal change has been called the blood oxygen level–dependent contrast effect. The sensorimotor cortex in the region of the upper genu of the central sulcus can be identified reliably as an activation site when observing CBF changes elicited by simple finger motor tasks (1–3). When the participant is unable to perform

voluntary motion regularly or rapidly enough to produce adequate activation, tactile stimulation of the hand will produce the desired activation in the region (4). Toe or foot movement less reliably produces the activation expected in the sensorimotor cortex near the interhemispheric fissure. One reason may be that head motion produced simultaneously with the toe task results in artifact and image degradation (5). Tongue movements produce activation in the lower portion of the sensorimotor cortex, usually in association with artifacts. The movement of the tongue and lips may generate significant artifact by altering the shim of the magnetic field (6). Identification of the activation from lip, tongue, and toe tasks has been less reliable because of artifacts.

One strategy to improve the detection of activation in the presence of motion artifact is the sin-

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Received November 18, 1998; accepted after revision July 21, 1999.

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gle-event paradigm (7). With this technique, short duration tasks are used and blood flow changes are monitored after completion of the task and cessation of motion. Stimulus-correlated motion artifacts are avoided by temporally segregating the motion and the blood flow changes that follow the task by several seconds. This technique has improved the detection of activation secondary to swallowing and speaking (8). The purpose of this study was to determine whether the single-event paradigm improved the identification of functional MR imaging activation from toe or tongue motion. We attempted to compare activation patterns from finger, tongue, and toe motion by using the single-event technique with those observed using the block-trial technique. We hypothesized that, for finger movement, the block-trial method would be superior because event-related motion would be minimal. Because the tongue and toe tasks are associated with motion artifacts, the single-event paradigm hypothetically might show more activation.

## Methods

### *Participants*

Six healthy volunteers (three men and three women), ranging in age from 25 to 30 years, were recruited as participants. All participants completed the Edinburgh Handedness Inventory and were strongly right-handed. Exclusion criteria included a history of psychiatric illness, seizures, substance abuse, and serious head injury. All participants provided informed consent according to institutional guidelines.

### *Imaging Procedures*

Functional MR imaging was performed using a commercial 1.5-T scanner (Signa; General Electric Medical Systems, Milwaukee, WI) equipped with a prototype 30.5-cm internal diameter three-axis local gradient head coil and an elliptical end-capped quadrature RF head coil. Each participant was positioned on the gantry with his or her head in the coil and with foam padding placed around the head to limit head motion within the coil. Scanning included sagittal images obtained with standard spin-echo pulse sequences and the following imaging parameters: field of view, 24 cm; 600/10 (TR/TE); flip angle, 90°; section thickness, 10 mm; and matrix, 256 × 128. These standard images were used to locate positions for three axial image planes used for functional imaging. These planes were located 5, 15, and 25 mm caudal to the vertex of the skull.

Functional MR images were acquired with a single-shot, blipped, gradient-echo, echo-planar pulse sequence (1). Each image had a 10-cm thickness, a 64 × 64 matrix, and a 24-cm field of view (voxel dimensions = 3.75 × 3.75 × 10.0 mm). The interscan interval (TR) was 1 second for both the single-event and block-trial methods. Each participant performed a standard finger-tapping task, a tongue motion task, and a toe movement task twice. For one performance of the task, data were acquired using a conventional block-trial and, for the other, a single-event methodology. For the block trial, a series of 165 sequential images was collected simultaneously for each of the three 10-mm contiguous axial sections. The participant was instructed to perform the task when cued at a rapid self-timed rate during each task period. The task periods were 15 seconds in length and were separated by 15-second periods of rest. Five periods of task and six of rest were included in the acquisition. The beginning and end of each task period was

signaled by cues presented over a pneumatic audio system. For the single-trial paradigm, a series of 315 sequential images was collected simultaneously from each of the three 10-mm contiguous axial sections. The participant was asked to perform the task 21 times, at 15-second intervals, when cued by the investigator. For the finger task, participants apposed the thumb and first finger bilaterally; for the tongue task, they repeatedly licked their lips; and for the toe task, they moved the toes bilaterally. The participants were instructed to keep their eyes closed throughout the scanning series.

### *Image Analysis*

The method used to generate functional images by the block-trial method from functional MR imaging data has been described in detail elsewhere (1). Briefly, functional images were generated off-line on a workstation using software analysis programs that were custom-written at our institution. The signal intensity was plotted for each pixel as a function of time. The correlation coefficient between the signal intensity time course and a reference function was calculated for each pixel. Pixels with a correlation coefficient greater than 0.50 (corresponding with the Bonferroni-adjusted alpha level of  $P = 2.4 \times 10^{-5}$ ) were superimposed on an anatomic image by interpolating both the functional and anatomic images to 256 × 256 pixels. The processing of images from the single-event paradigm has been described (7, 8). In this method, the reference function, with a change from baseline every 6 seconds after each task, is compared with the time course plot. Signal intensity changes attributable to motion just before the blood flow change are excluded from the cross correlation. Pixels with a correlation coefficient of 0.50 were selected and superimposed on the anatomic images.

Two investigators reviewed the functional images and counted the number of activated pixels in each section and in each participant. The activated pixels were classified as belonging to the sensorimotor cortex (motor), to the supplementary motor area (SMA), or to neither of these areas by means of standard parcellation methods (9). For the toe task, activation that was near the central sulcus and the interhemispheric fissure was classified as motor. For the finger-tapping task, activation near the superior genu of the central sulcus was classified as motor. For the tongue task, activation near the central sulcus and the sylvian sulcus was classified as motor. Whenever a cluster of pixels was obtained, each one was counted and classified. Activated pixels near the midline anterior to the sensorimotor cortex were classified as being in the SMA. Pixels that were not in either of these two regions were classified, for the purposes of this study, as nonspecific.

For both the single-event and multiple-event paradigms, the activated pixels in and outside the sensorimotor cortex and SMA were counted. The percentage of pixels in the sensorimotor cortex in relation to all pixels was calculated for each task and each volunteer. Differences between the two acquisition paradigms were tested using the standard *t* test, and significance was set at the  $P < .05$  level.

## Results

Activation in the sensorimotor cortex or SMA was identified in each volunteer (Fig 1, Table 1). For the finger and tongue tasks, activation was shown consistently in the sensorimotor cortex with both the single-event and the block-trial methods. For the toe task, activation was shown by the block method in five of the six participants and by the single-event method in three.

Consistently for the finger movement, the tongue movement, and the toe movement tasks, more activated pixels were identified by the single-event

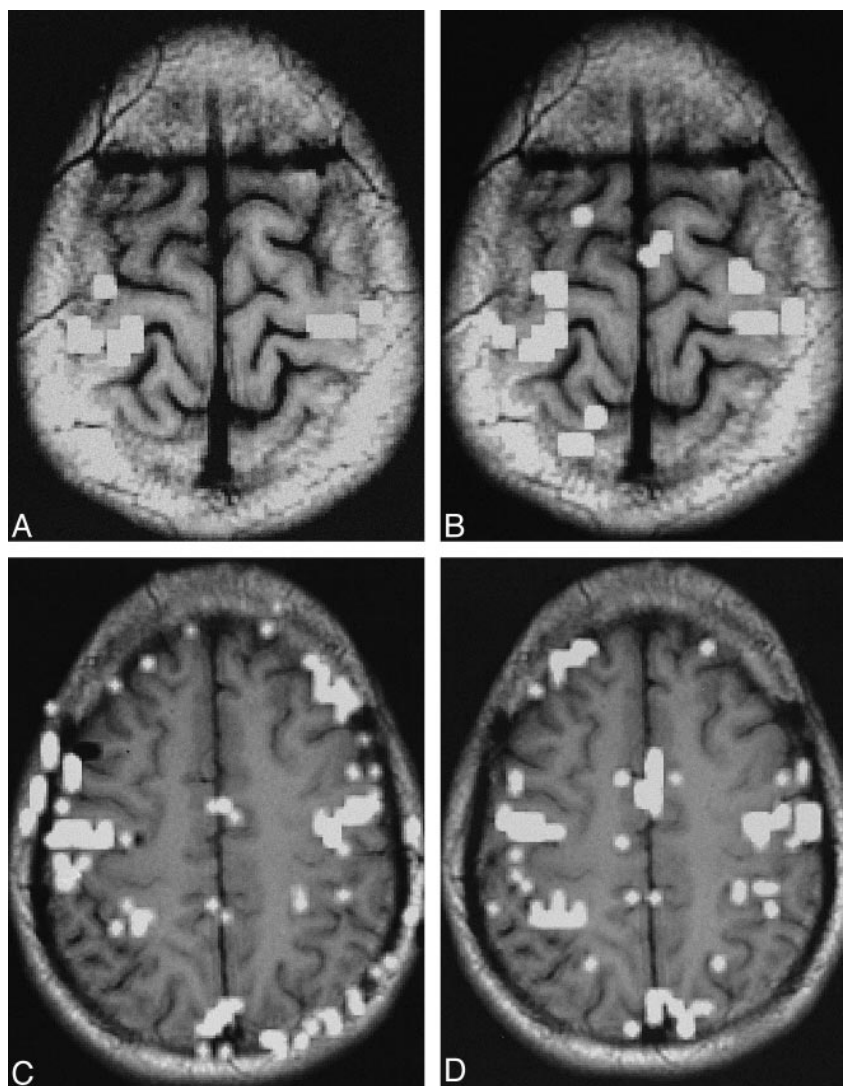
FIG 1. Comparison of the block-design method and the single-event method for one participant.

A, Analyzed by the block-design method, the finger task shows activation in the sensorimotor cortex and (in an adjacent section that is not illustrated) in the midline in the presumed SMA.

B, Analyzed by the single-event method, the finger task shows activation in the sensorimotor cortex, SMA, and parietal and frontal lobes, which was classified as non-specific in this study.

C, Analyzed by the block-design method, the tongue task shows activation in the inferior sensorimotor cortex on the convexity and in the SMA in the midline. Activation along the inner table over the left parietal lobe is likely motion artifact.

D, Analyzed by the single-event method, the tongue task produces activation in the SMA and sensorimotor cortex and in frontal and parietal regions. The motion artifact is less evident.



than by the block-trial paradigm (Fig 2). Overall, an average of 25% more pixels were identified within the sensorimotor cortex by the single-event method than by the block-trial method. The number of activated pixels outside both the motor region and SMA was also higher with the single-event paradigm for each of the three tasks studied.

The percentage of activated pixels that were identified in each area is shown graphically in Figure 3. For the finger movement task analyzed by the conventional block-trial method, an average of 84% of all activated pixels were in the sensorimotor cortex. For the single-event method, 45% of activated pixels were in the sensorimotor cortex. This difference was significant at the .014 level. Using the block-trial method, an average of 4% of pixels was not classified in either the SMA or sensorimotor cortex for finger movement. With the single-event paradigm, 41% were so classified.

For the tongue task, both the single-event and block-trial methods produced a similar average percentage of activated pixels in the sensorimotor cortex (32% or 30%). This difference was not signif-

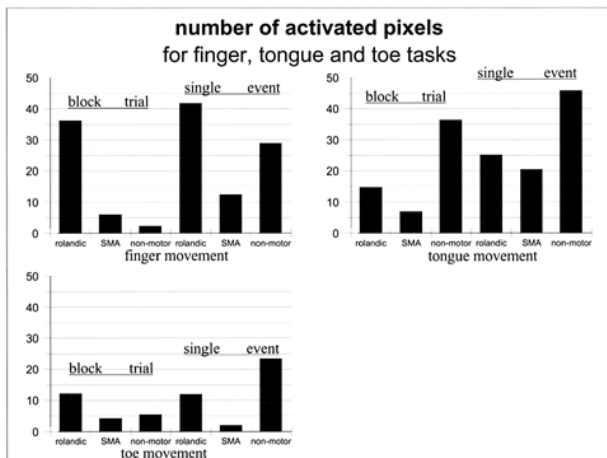
icant. For the toe movement task, the average percentage of activated pixels that were in the sensorimotor cortex was 55% for the block method and 37% for the single-event method. The difference was not significant. For both the tongue and the toe tasks, the percentage of pixels outside the SMA and sensorimotor cortex was greater for the single-event paradigm than for the block method.

### Discussion

This study shows that, compared with the block-trial method, the single-event method of measuring activation secondary to motor tasks revealed a greater number of activated pixels both within and outside the motor cortex. The single-event method produced a lower percentage of activated pixels that were specific to the primary motor region for all tasks. For the finger movement task, which does not usually produce head motion artifacts, the block-trial method generally produced a greater percentage of activated pixels in the sensorimotor cortex or SMA than did the single-event method.

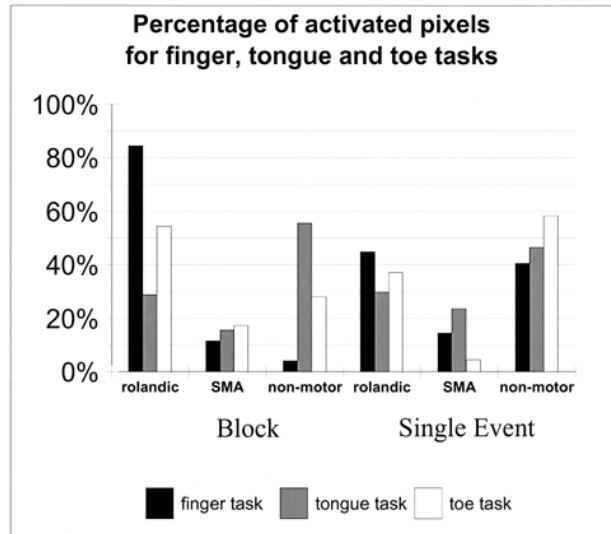
**Number of activated pixels for each subject, each task and each region**

Subject	Block Method			Single-Event Method		
	Rolandic	SMA	Non-motor	Rolandic	SMA	Non-motor
Finger Task						
LW	11	2	0	8	11	30
MJ	12	1	0	2	1	50
SB	20	2	3	34	16	50
MS	55	16	3	62	10	0
MM	77	14	8	73	28	5
OH	42	1	0	72	8	39
AVG	36.2	6.0	2.3	41.8	12.3	29.0
Tongue Task						
LW	gw	4	16	20	30	42
MJ	5	2	0	15	7	4
SB	8	4	22	12	26	62
MS	14	13	65	15	21	48
MM	28	11	51	60	19	52
OH	33	7	64	28	19	67
AVG	14.7	6.8	36.3	25.0	20.3	45.8
Toe Task						
LW	14	0	0	16	2	29
MJ	0	3	0			
SB	19	12	8	13	0	8
MS	11	3	15	7	4	33
MM	13	6	9			
OH	16	1	0			
AVG	12.2	4.2	5.3	12.0	2.0	23.3



**FIG 2.** Average number of activated pixels within the sensorimotor cortex and SMA and outside these regions for each task and each analysis method.

For the tongue movement and the toe movement tasks, which may produce head motion artifacts, the single-event paradigm provides a useful alternative to the block-trial method for identifying the sensorimotor cortex or SMA. For any of these motor tasks, the single-event method did not achieve greater specificity for primary motor areas. With either the block design or single-event method, activation secondary to the toe task was not shown consistently.



**FIG 3.** Percentage of activated pixels in the sensorimotor cortex region, in the SMA, and outside of these two areas.

The single event-imaging paradigm functions most effectively for stimuli that recur and have a readily detectable effect on the time course plots. Event-related functional MR imaging has been used to map transient hemodynamic responses to cognitive tasks and stimuli (10–14). With it, paradigms identical to those used in behavioral evoked response potentials and single-unit physiologic studies can be used. Neuronal stimuli lasting only a few 10s of milliseconds and individual events associated with small responses can be detected. Because it measures signal intensity changes over short time periods, the single-event method is less susceptible to baseline drift than is the block-trial method. In theory, the single-event method provides better detection of activation than does the block method when the stimuli are associated with motion because the motion can be detected and disregarded. The single-event paradigm produces less significant correlations than the block method when each iteration of the stimulus causes sustained changes in signal intensity. With the single-event method, we used 21 iterations of the task to generate adequate signal-to-noise ratios and allowed sufficient time (15 seconds) between tasks for the hemodynamic response to return to baseline (10).

The comparison of the block-trial and the single-event methods cannot be generalized to all tasks on the basis of this study. The tasks chosen for this study included the finger-tapping task, with which motion is not usually a problem, and tongue and toe tasks, with which motion artifacts are a problem. The tongue task, analyzed with the block-trial paradigm, usually produces artifacts, likely resulting from changes in the magnetic field as parts of the face outside the field of view are moved (6). With the toe task, motion artifact is caused by head and foot movement. Activation patterns with the single-event paradigm may not resemble exactly the patterns with the block-trial method (7, 8, 11).

The decrease in percentage of “specific” motor activation may be from a reduced statistical power because of the shorter hemodynamic response. It may also represent true activation outside the motor cortex, which, because of its transient nature, is better detected with the single-event method. Because only the activation within the sensorimotor cortex helps to localize this region, greater activation outside this region lacks specificity for surgical planning. The sensitivity of the block-design method and the single-event method may differ from one motor region to another because the location or time course of the hemodynamic response may differ. Specifically, the hemodynamic response in basal ganglia secondary to motor tasks may be less prolonged than in the sensorimotor cortex (15). The location and duration of the hemodynamic response from a self-paced and a cued activity may differ.

This study was designed primarily to compare the single-event method with the block-trial paradigm for identifying the primary motor regions. For the block trial, we used a conventional boxcar reference function rather than a more sophisticated hemodynamic model of the response. We chose a threshold empirically to balance type one and type two statistical errors without attempting to achieve a full correction for statistical comparisons. The study was limited to one threshold that is commonly used in functional studies. Selection of a lower threshold would likely increase the number of nonspecific activations. Use of a higher threshold would decrease the number of pixels identified, increase the number of cases in which no activation was identified, and unlikely increase the fraction of activated pixels within the primary motor cortex.

### Conclusion

The single-event method is an alternative to the block-trial method for studying activation secondary to motor tasks. For the tongue and toe movement tasks, which may produce head motion artifacts, the single-event paradigm may reveal activation, although not with a greater specificity for the sensorimotor cortex and SMA. For the fin-

ger movement task, which does not usually produce head motion artifacts, the block-trial method generally produces a greater percentage of activated pixels in the sensorimotor cortex and SMA than does the single-event method.

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