MEG Reveals Different Contributions of Somatomotor Cortex and Cerebellum to Simple Reaction Time After Temporally Structured Cues

Tim Martin,¹ Jon M. Houck,¹ Joel Pearson Bish,² Dubravko Kičić,³
C. Chad Woodruff,⁴ Sandra N. Moses,⁵ Dustin C. Lee,¹ and
Claudia D. Tesche¹

¹Department of Psychology, University of New Mexico, Albuquerque, New Mexico, USA

²Department of Psychology, Ursinus College, Collegeville, Pennsylvania, USA

³BioMag Laboratory, Engineering Centre, Helsinki University Central Hospital, Helsinki, Finland

⁴Center for the Neurobiology of Learning and Memory, University of California,
Irvine, California, USA

⁵Rotman Institute, Toronto, Ontario, Canada

Abstract: Magnetoencephalography (MEG) was used to measure brain activity while participants performed a simple reaction to targets after either a random interval (uncued targets) or a series of isochronous warning stimuli with 200-ms intervals that acted as a countdown. Targets could arrive “on time” or “early” relative to the preceding warning stimuli. Cerebellar activity before any stimulus onset predicted uncued simple reaction time. Onset of activity in somatomotor cortex relative to the target predicted reaction time after two warning stimuli when the target arrived on time or early. After three warning stimuli, when the target arrived on time and was certain to occur, prestimulus cerebellar activity and somatomotor onset were significant predictors of reaction time. When the target arrived early after three warning stimuli, prestimulus cerebellar and cingulate activity were predictive. The cerebellar results may reflect a number of possible factors, including a role in timing, response readiness, prediction and attention. *Hum Brain Mapp* 27:552–561, 2006. © 2005 Wiley-Liss, Inc.

Key words: MEG; reaction time; entrainment; timing; auditory; motor

INTRODUCTION

Human and other cognitive systems are not passive signal receivers, but actively seek out, anticipate, and prepare for input and behavior. This requires not only attending to the correct source of information and preparing to emit the correct behavior, but also doing so at the appropriate time. It is now well established that symbolic temporal information [Coull and Nobre, 1998; Nobre, 2001] and temporal structure [Boltz, 1991; Jones, 1976; Jones and Boltz, 1989; Jones and Yee, 1997; Klein and Jones, 1996; Klemmer, 1956; Large and Jones, 1999] cause behavioral benefits and deficits consistent with the concepts of temporally allocated preparation and

Contract grant sponsor: Mental Illness and Neuroscience Discovery Institute, Albuquerque, NM.

*Correspondence to: Tim Martin, University of New Mexico, Logan Hall, Albuquerque, NM 87131. E-mail: tma2010@yahoo.com

Received 31 January 2005; Accepted 11 July 2005

DOI: 10.1002/hbm.20200

Published online 24 October 2005 in Wiley InterScience (www.interscience.wiley.com).

attention. Humans have been shown to take advantage of local temporal structure even in random sequences [Rabbitt and Vyas, 1980].

Such preparatory processes have been studied extensively, most commonly using chronometric measures of behavior. Cognitive models of reaction time (RT) generally posit a number of component processes or stages, such as sensory registration, target recognition, response preparation, and response execution. Such stages serve as sources of variance for statistical models of RT, which may differ in the number of asserted stages, whether they are serial, parallel, or some combination of the two, and in the probability distributions of event timing of each stage [for a review, see Luce, 1986]. Under the simplest assumption of strictly serial processing, response latency should be the sum of the processing and transmission times of each stage [Sternberg, 1969]. In the case of multiple parallel pathways, each with its own set of components, response latency is the sum of processing and transmission times along the so-called critical path. More likely, stages along a particular path are not strictly serial. Rather, later stages probably begin processing with only partial information from earlier stages, and responses are initiated after some threshold of activation is reached by the response generation stage. In addition, feedback from later stages back to earlier stages is thought to occur. Preparatory processes are thought to modulate some or all of the stages of a particular model by increasing information processing efficiency and reducing the time necessary for a stage to complete its contribution to RT [Miller and Hackley, 1992].

The present study is intended to investigate the process by which temporal structure mediates preparation by observing brain activity with magnetoencephalography (MEG) while participants produce speeded simple reactions to targets, with and without temporal cueing. Characteristics of the estimated neuronal current are then expected to account for variability in simple RT (SRT). The basic design is a variant on the warning stimulus (WS) paradigm [Klemmer, 1956], in which a WS informs observers that a target is about to occur. To induce temporal structure, we use series of two or three isochronous WS. Most targets then occur at a latency equal to the inter-onset interval (IOI) between WS (i.e., they are validly cued by the temporal structure of WS), whereas a minority of cases occur early (i.e., they are invalidly cued). Behavioral experiments with this paradigm using choice RT (CRT) as a dependent measure indicate that the benefit to response latency from the cues cannot be accounted for solely by elapsed time and conditional target probability [Martin et al., 2005].

Presumably, the effects of preparatory processes are mediated in the nervous system by increased activation levels in structures relevant to the processing of stimulus and response [Desimone and Duncan, 1995], changes in gain [Hillyard et al., 1998], inhibition of activity in structures irrelevant to the processing of the expected stimulus and response [Skinner and Yingling, 1977], or some combination of these. This has the effect of decreasing the time needed to

integrate inputs and generate a population response, and may also reduce the temporal variability of the neuronal population response. Onset times and duration of activity are expected to be predictors of RT. For example, presumably the earlier the motor cortex begins to prepare and execute a response, the earlier the response will occur. The shorter the duration of response preparation before the efferent volley from motor cortex to effectors, the earlier the response should occur. One would expect further that later stages are better predictors than are earlier stages, because there are fewer sources of variance between later stages and muscle contraction. Given a sufficiently large sample, the onset and duration of each stage of processing should make a unique contribution to the prediction of RT, but in practice the ability to predict RT will depend in part on variability of sources of variance downstream from a given source. It should be possible in this experiment to account for variance from brain sources, but after the efferent volley from motor cortex, the variability in transmission times through the spinal ganglia and down the arm to the finger are not accessible using our methods.

There is also a growing awareness that activity immediately preceded an experimental trial influences performance. Brandt et al. [1991] found that α power was positively associated with N1 amplitude. Haig and Gordon [1998] found that prestimulus α phase synchronicity was associated with both a greater N1 amplitude and faster reactions. Linkenkaer-Hansen et al. [2004] found differential patterns of association between prestimulus oscillatory activity and signal detection performance over somatosensory and parietal regions using MEG. Such prestimulus activity may reflect more tonic cognitive states such as arousal or vigilance.

Several structures may be hypothesized to be involved in mediating temporally structured cueing. Clearly the primary sensory cortex would be a candidate [Mäkinen et al., 2004; Tiitinen et al., 2005], as would the somatomotor cortex. The modulation one would expect from these structures is an earlier latency of either onset or peak after temporal cueing. One might also expect a change in peak amplitude, but our design does not allow us to rule out other determinants of such a peak change, most notably habituation.

Slow potential shifts are also likely to play a role in mediating the effects of temporally structured cueing. For example, the contingent negative variation [CNV; Walter et al., 1964] is a slow shift observed in evoked electric potential difference observed between a WS and a target requiring some response. Its counterpart in biomagnetic data is the contingent magnetic variation [CMV; Elbert et al., 1994]. Generation of CNV- and CMV-type responses is believed to result from slow changes in neuronal activity in multiple brain areas. Elbert et al. [1994] observed CMV activity with a MEG array that covered half of the scalp, but were unable to identify source locations for this activity. They concluded that several sources were likely contributors to the slow CMV shift. Using a twin 37-channel whole-head MEG array in two participants and a 151-channel whole-head array on a third, Dammers and Ioannides [2000] observed sources for

a CMV response in primary sensory, posterior parietal, inferior prefrontal, and sensorimotor cortices during a go/no-go task, but noted considerable intersubject variability in the locations of these sources. Using functional magnetic resonance imaging (fMRI), Nagai et al. [2004] identified activity in primary motor cortex, supplementary motor area, somatomotor cortex, midcingulate cortex, bilateral insula, dorsal thalamus, and dorsal medial cerebellum during the foreperiod separating a WS from a target. Bares and Rektor [2001] also reported CNV-like responses using depth electrode recordings located in basal ganglia structures in humans. Interestingly, Tesche and Karhu [2000] observed a similar CMV-like slow shift in cerebellar activation after omission of anticipated somatosensory stimuli in a paradigm that did not call for an explicit motor response.

Structures that are engaged in the processing of temporal information may also mediate temporally structured cueing, although not necessarily those areas involved in processing symbolic temporal information per se. Of particular relevance to this experiment, the cerebellum has been implicated in computations on temporal structure [Ivry and Keele, 1989; Mangels et al., 1998], anticipation [Tesche and Karhu, 2000] and attention [Allen et al., 1997; Courchesne and Allen, 1997]. The cerebellum has long been implicated in adaptive control of motor movements and may also contribute to predictive control of cognitive processes [c.f. Ito, 1984, 2005]. To the extent that predictive components of adaptive control are combined with temporal information processing, the cerebellum would be a prime candidate for mediating the effect of temporally structured cueing on RT.

We used MEG to investigate brain dynamics associated with temporally structured cueing. We hypothesized that temporal structure would cause an earlier onset of activity after a target in sensory and motor areas corresponding to faster reactions, and that these onset times would predict response latency. We further hypothesized that a slow shift, similar to a CNV/CMV, would be observed in those sources associated with the perception of and response to targets. Finally, we explored the possibility that prestimulus activity in some sources would be associated with response latency, using a novel approach by characterizing such activity with a measure of variability.

SUBJECTS AND METHODS

Subjects

This experiment complied with the standards of human research as explained in the Declaration of Helsinki, and was approved by the relevant Institutional Review Boards. Eleven normal adult volunteers (3 women) participated in this experiment. Two were excluded from further analysis. In one case, the participant failed to respond to any uncued SRT trials. In the second case, the participant reported difficulty maintaining an alert state, and inspection of the behavioral data confirmed that this participant failed to respond for extended periods of time. Of the remaining nine participants, six were members of the experimental partici-

Figure 1.

Illustration of experimental conditions.

pant pool at the BioMag laboratory, and three were coauthors of this study. The mean age was 25.8 years (range, 20.6–31.5) and two participants were left-handed. All participants had participated previously in neuroimaging experiments.

Procedure

Figure 1 illustrates each task condition. Stimulus presentation was controlled by *Presentation* software on a desktop PC. Trials were mixed and presented in a different random order for each participant. Intertrial intervals were varied randomly between 300 ms and 700 ms using a uniform probability distribution. On each trial, participants were presented with no, two, or three 256-Hz WS, followed by a 512-Hz target tone. The duration of all stimuli was 100 ms, with an intensity of approximately 87.1 dB (A-weighting) and 10 ms rise and fall times. All WS were separated by a constant IOI of 200 ms, corresponding to a stimulus input frequency of 5 Hz. On 100 trials, there was no WS, a condition referred to as uncued. On 400 trials (67% of the trials with two or three WS), the target occurred with an IOI of 200 ms after the last WS. This is termed the on-time condition. On 200 trials (33% of the trials with two or three WS), the target occurred with an ISI of 100 ms, which we term the early condition. The design can be conceived as a 2 (number of WS) $\times$ 2 (target IOI, 100 or 200 ms) repeated-measure factorial with one hanging cell: the uncued condition has no comparison across the target IOI dimension.

Participants were informed that on most trials, the target would be on time relative to the pulse established by the WS, but that on some trials the target would occur early. Participants were asked to respond with a button press to the target tone, and both speed and accuracy were emphasized.

The magnetic field outside the head was measured in a magnetically shielded room with a 306-channel VectorView MEG array (Vectorview, Elekta Neuromag Ltd.), sampling at 600-Hz and band-pass filtered at 0.1 to 200 Hz. Responses

were recorded by *Neuromag* acquisition software from a nonmagnetic button box.

Data Analysis

For each participant, all anticipatory responses ($RT < 0$ ms) were removed, resulting in the loss of less than 1% of data in all cases. An overall mean RT and standard deviation (SD) were calculated. All observations falling more than three SD from the mean were removed from further analysis before calculating condition-specific means. This procedure resulted in the removal of <3% of observations for all participants. All tests of statistical significance were two-tailed unless otherwise specified.

Because target IOI does not have any meaning for uncued SRT trials (i.e., a target cannot arrive early or on time relative to a random inter-trial interval), this design is not a full factorial. We therefore analyzed each measure with two analyses of variance (ANOVA) that served as planned contrasts with a Bonferroni corrected α of 0.025. To test the effect of time markers, a three-level (uncued, two WS, and three WS) multivariate repeated-measure ANOVA was used. To test the effect of target IOI, the second contrast was a 2 (number of WS) $\times$ 2 (target IOI) ANOVA that included trials with two or three WS and targets occurring early (1/2 ISI after the last WS) or at expectation.

The MEG data for all gradiometer and magnetometer sensors in the array were averaged in each condition over the epoch beginning 100 ms before onset of the first stimulus and ending 900 ms after onset of the last stimulus. Blink and heart artifacts were removed using signal-space projection [SSP; Uusitalo and Ilmoniemi, 1997]. These averages were then baseline-corrected using a 100-ms epoch immediately before the onset of the first stimulus, and low-pass filtered at 45 Hz, width 5 Hz. One participant's data was also high-pass filtered at 0.5 Hz, width 1 Hz, to remove a remaining low-frequency artifact. Visual inspection was used to identify and remove channels with excessive noise. This resulted in the removal of one channel in the data of seven participants, two channels in one participant's data, and 10 channels in one participant's data.

Dipole approximations to current sources were found for the averaged data using an iterative fitting procedure (for a general discussion of multidipole fits, see Hämäläinen et al. [1993]). In step 1, initial dipole locations were found for the three-WS, on-time condition over an epoch from the onset of the first WS to 900 ms after the presentation of the target stimulus. A visual search was carried out for features that were represented at a sampled point as a dipolar field pattern with a prominent peak response in nearby sensor waveforms. For the bilateral left and right auditory sources, only channels in the corresponding hemisphere were used during this procedure. In step 2, the set of all identified dipoles was subjected to an iterative multidipole least-squares fitting procedure to optimize individual source locations/orientations using the *Neuromag Elekta* software. Variance accounted for by the set of all identified dipoles was removed from the evoked response data using SSP and epochs of

poor goodness-of-fit were inspected for additional sources following the procedure described in step 1. Step 2 was repeated until the goodness-of-fit for all peak responses exceeded 90%, and remaining epochs with poor goodness-of-fit seemed to contain no further obvious dipolar signals.

Dipole source locations were examined across subjects for the presence of common regions of activation. If a region of activation (i.e., primary motor cortex, medial cingulate cortex, and cerebellar vermis) was identified in eight of nine participants, a single additional dipole "seed" near a comparable location was included in the set of all sources for the ninth participant. A subsequent multidipole least-squares fit was conducted for this subject with the expanded set of sources. If the location of the seeded dipole remained within a centimeter of the original site, it was retained in the analysis and identified with the brain area under consideration. If the location of the dipole changed by more than 1 cm, the source was retained in the analysis but not identified with the brain area under consideration. There were no criteria for the amplitude of the waveform for this source, because a waveform that reflected only measurement noise would be expected to contribute only measurement error to subsequent analyses.

After determining a set of sources for each subject that included the common sources mentioned above for the three-WS condition, we reoptimized the dipolar locations/orientations for all conditions and participants using a multidipole least-squares fit. Optimization was conducted separately for each condition for an epoch starting from onset of the first stimulus to 900 ms after onset of the last stimulus. Variability of dipole locations between conditions was estimated using the distance of each dipole from the center of the reference frame, as this measure summarizes variability in all three dipole coordinates. Waveforms for the amplitude of current flow for all of the common sources were extracted from the multidipole fits for each subject and condition for further analysis.

Measures of onset latency and prestimulus (baseline) activity were derived from the waveform estimates for each subject, condition, and source. Onset latency was derived by squaring each waveform and calculating the standard deviation of the baseline epoch of the squared waveform. Onset of a source was then defined as the first deviation after the first stimulus that was greater than three standard deviations of the squared baseline epoch. Post-target onset was defined as the first deviation of the squared waveform after the target that was greater than three standard deviations of the baseline. These two measures are identical for the uncued condition.

To obtain a measure of prestimulus activity from averaged evoked responses, the mean estimated current is not appropriate, because the baseline correction artificially constrains the mean measured magnetic flux during the baseline epoch to zero for each sensor. Because baseline correction does not affect the variability of the measured field over time, the standard deviation of waveform activity was computed over the baseline epoch (from 100 ms before the first

Figure 2. Mean reaction times and 95% confidence intervals. **A:** Means for the three-level ANOVA testing the effect of warning stimuli (WS). **B:** Means for the 2 (number of WS) $\times$ 2(target inter-onset interval [IOI]) ANOVA testing the effect of target IOI. Circles, early targets (target IOI = 100 ms); diamonds, on-time targets (target IOI = 200 ms).

stimulus to onset of the first stimulus), using the filter settings described above. The assumption was that this variability would reflect ongoing activity that is not necessarily phase-locked with the stimuli, but may nevertheless be related to task performance.

RESULTS

Behavioral Data

A plot of the mean RTs in each condition is presented in Figure 2. The three-level repeated-measure ANOVA revealed a main effect of WS ($F[2,7] = 63.287$, $P < 0.0005$). As indicated in Figure 2A, cued SRT was over 100 ms faster than uncued SRT. The 2 (number of WS) $\times$ 2 (target IOI) ANOVA revealed a main effect of WS ($F[1,8] = 53.249$, $P < 0.0005$), and a main effect of target IOI ($F[1,8] = 11.557$, $P = 0.009$). The interaction was not significant. Figure 2B indicates that three WS caused faster reactions than two WS did, and targets occurring on time relative to the WS were responded to faster than were targets appearing early.

MEG Data

The dipole fitting procedure resulted in models containing between 8–12 dipoles. For the epoch between 0 ms (target onset) and 400 ms, the mean peak goodness-of-fit (gf_{peak}) = 92.28, ranging between 77.79–97.46. Seven sources were located consistently between observers using this procedure: sources in left and right auditory cortex for the P50m and N100m response bilaterally, a source in or near primary motor cortex, a medial cingulate source, and a source in medial cerebellum. Table I presents averaged variability of each common dipole location between conditions, collapsed across subjects. The average variability was <6 mm in all cases. Figure 3 shows examples of the common source locations and orientations for a single subject and the associated grand-averaged waveforms. A CMV-like slow wave of increasing activity was visible after the first WS in each of the seven common sources, although it was less prominent in the medial cingulate source.

Onset latency and post-target onset latency for each source were analyzed with two ANOVAs in the same way that behavioral data was analyzed. Onset latency was not significantly affected by condition. For post-target onset latency, the somatomotor source ($F[2,7] = 9.633$, $P = 0.01$) and right N100 source ($F[2,7] = 15.80$, $P = 0.003$) were active more quickly after cued than uncued targets. This pattern, although present in each of the other sources, was not significant in any other source. The 2 (number of WS) $\times$ 2 (target IOI) ANOVA failed to reveal any significant differences in these measures of brain dynamics.

The distribution of post-target onset times after cueing for the somatomotor source was positively skewed. Inspection of the distribution revealed that this source was already active when the target occurred for six participants in both the two WS and three WS on time conditions. This causes a violation of the linearity and homogeneity of variance assumptions of the product moment correlation. Although correlation is normally robust to these violations [Cohen and Cohen, 1983], with such a small sample they might introduce considerable bias into parameter estimates and tests of significance. We therefore took two approaches to analyze this source further. First, we transformed the onset times into a categorical grouping variable (0 ms and >0 ms), and carried out independent sample *t*-tests on the RTs for the

TABLE I. Averaged standard deviations of common dipole locations

Source	Min	Max	Mean
Left P50m	1.11	4.92	2.5238
Right P50m	0.93	6.09	3.0265
Left N100m	1.81	7.67	3.3594
Right N100m	0.64	5.11	2.5541
Somatomotor	0.99	6.27	3.4607
Cerebellum	1.18	11.76	5.277
Cingulate	0.99	4.65	2.7148

Standard deviation of each dipole location for the five conditions was calculated for each participant, then averaged across participants. Units = mm.

Figure 3.

Responses determined from the MEG data for activity in left auditory cortex (**A**; P50m), left auditory cortex (**B**; N100m), somatomotor cortex (**C**), midline cerebellum (**D**), and midline cingulate cortex (**E**). MR images on the left show source locations and orientations for a single subject. Waveforms on the right show response amplitudes averaged across all nine subjects for the

“uncued” condition and for “on time” trials with two and three warning stimuli (WS). The dotted vertical lines indicate onset times for the auditory warning stimuli. The solid vertical line indicates target onset time. The first WS occurs at -600 ms for the three-WS on-time condition, and at -400 ms for the two-WS on-time condition. Target onset is at 0 ms for each condition.

two WS and three WS on time conditions. This has the advantage that the predictor variable is only assumed to be nominal, but carries the cost of a reduction in range that attenuates the correlation. Somatomotor onset significantly affected RT after two WS when the target arrived on time

($t[7] = 3.236$, $P = 0.007$, one-tailed). After three WS, when the target arrived on time, the effect was also present although smaller ($t[7] = 1.948$, $P = 0.046$, one-tailed).

Secondly, we developed another measure that we call target-related onset time, again using the squared wave-

TABLE II. Correlations between brain dynamics and RT

	Uncued	2 on	3 on	2 early	3 early
Somatomotor onset	0.508	0.768 ^b	0.669 ^a	0.784 ^a	0.455
Cerebellum onset	-0.302	-0.012	0.145	0.667 ^a	0.220
Cingulate onset	0.019	0.588	0.093	0.610	0.267
Somatomotor baseline SD	-0.133	-0.394	-0.187	-0.309	-0.325
Cerebellum baseline SD	0.931 ^c	0.413	0.867 ^b	0.355	0.768 ^a
Cingulate baseline SD	0.658	0.651	0.491	0.225	0.710 ^a

Onsets refer to target-related onsets.

^a $P < 0.05$; ^b $P < 0.01$; ^c $P < 0.001$.

SD, standard deviation.

form. For sources that were inactive (amplitude below 3 SD of the baseline mean) at target onset, this measure was identical to post-target onset latency. For targets already active when the target occurred, we worked backward to the deviation that most closely preceded target onset.

Correlations between RT and selected measures of source dynamics are presented in Table II. Scatter plots of significant correlations are presented in Figure 4. In general, there was no consistently detectable pattern of linear correlation between sensory source onset times or baseline standard deviations and SRT. Cingulate baseline variability was a significant predictor of SRT only for early targets after three

WS. The two measures of brain activity showing the most consistent relationships with SRT were cerebellar baseline standard deviation and somatomotor source target-related onset time. Cerebellar baseline SD was significantly related to uncued SRT and SRT after three WS, whether the target arrived on time or early. Somatomotor onset was a significant predictor of SRT after two or three WS when the target arrived on time.

From the scatter plots, there seems to be what might be considered outliers at the upper end of each plot. To evaluate the impact of potential outliers, we defined outliers to be observations lying outside of two standard deviations of the

Figure 4.

Scatter plots of significant correlations between somatomotor and cerebellar waveform measures reported in Table II.

mean of their distribution, and checked each of the measures involved in the significant correlations for outliers. We then removed any outliers and recalculated the product moment correlations. There were no outliers in the RT distributions. For the somatomotor source target-related onset latency, the longest latencies were outliers for the two WS on time ($z = 2.02$) and two WS early ($z = 2.26$) conditions. With these observations removed, the correlations between onset time and RT dropped to 0.65 ($P = 0.081$) and 0.784 ($P = 0.013$) for the two WS on-time and two WS early conditions, respectively. For the baseline SD of the cerebellar source, there was also one outlier in the uncued condition ($z = 2.01$), three WS on-time condition ($z = 2.50$) and three WS early condition ($z = 2.50$). With these outliers removed, the correlations between cerebellar activity and RT dropped to 0.913 ($P = 0.002$), 0.818 ($P = 0.013$) and 0.401 ($P = 0.325$) for the uncued, three WS on-time, and three WS early conditions, respectively.

DISCUSSION

There was a benefit to RT of time markers, as expected. Although these results are consistent with an explanation based on increasing probability of a target with increasing time since the first WS [Näätänen, 1970], Martin et al. [2005] have presented behavioral evidence that temporal pattern contributes variance to performance not accounted for by elapsed time.

We found a clearly discernible increase in activity for all cued conditions that began after the first WS and lasted until the evoked response to the target in all of the common sources: the bilateral auditory cortical P50m and N100m sources, medial cingulate and somatomotor cortex, and mid-line cerebellum. The observed slow increase of activity is similar to slow shifts (CNV and CMV) observed preceding movement cued by a single WS [Elbert et al., 1994; Walter et al., 1964]. The presence of the activity reported here across a constellation of sources is consistent with past literature on the CNV/CMV for a single WS cue [Dammers and Ioannides, 2000; Elbert et al., 1994; Nagai et al., 2004].

Our design used intervening stimuli between the initial WS and target. Direct comparison with previous CNV/CMV results for movement cued by a single stimulus thus is not possible. However, it seems likely that CMV-type waves observed in our data reflect activation of distributed sensorimotor and attentional networks that overlap those seen in alerting tasks. Our experimental design does not allow us to distinguish whether the observed slow shifts are due only to a mechanism initiated by the first WS, as in an alerting paradigm, or also reflects unique aspects of multiple temporally structured cues. Interestingly, slow shifts of activation have been observed previously in cerebellum with MEG in a somatosensory omission paradigm [Teschke and Karhu, 2000]. In these data, slow shifts occurred in cerebellar sources before the first stimulus that followed the random omission of a single stimulus in the train of stimuli. The presence of CMV-like slow shifts in both the visually cued movement data presented here and also in a somatosensory

omission paradigm that required no voluntary movement supports the concept that cerebellum may be involved in the processing of the temporal content of sensory input per se.

Temporally structured cueing decreased the post-target onset latency of somatomotor cortex and right auditory N100 source. This finding may be due in part to the CMV-like slow wave, and likely reflects the fact that these sources were active before target onset. The combination of a CMV-type wave and earlier onset is evidence of modulation of sensory processing consistent with increased activation in a structure relevant to the target stimulus [Desimone and Duncan, 1995], although this result certainly does not allow us to rule out gain or inhibition of irrelevant structures as contributors to the behavioral effects. The fact that the effect was not detectable for other sensory sources may be a statistical power issue, because each of the other sources had the same pattern.

We did not find evidence of modulation of brain dynamics as a function of target probability [Banquet and Contreras-Vidal, 1992], although the predictive power of prestimulus cerebellar dynamics and post-target somatomotor onset were generally not as good for targets occurring early relative to the WS series. This is likely due to the weakness of the probability manipulation. We used a 1/3 probability of an early (invalidly cued) target, in order to obtain an adequate number of invalid trials for signal averaging in a reasonable amount of time. Invalid cue probabilities of 1/4 or 1/5 are much more common in the attention literature [i.e., Mangun and Hillyard, 1991; Posner et al., 1980; Printzmetal et al., 2005]. A more intense manipulation of trial probability would be desirable to specifically investigate the effects of target probability.

To our knowledge, data presented here are the first to indicate that variability in cerebellar activity before stimulus onset is associated with RT. This relationship was maintained for the uncued and three WS on time conditions even when an outlier was removed, which reduced the range of this predictor and reduced the degrees of freedom, thus reducing statistical power. This finding adds to a growing literature on prestimulus correlates of performance [Brandt et al., 1991; Haig and Gordon, 1998; Linkenkaer-Hansen et al., 2004]. The interpretation of prestimulus cerebellar activity is more complex than that for somatomotor cortical onset. This measure was a significant predictor of uncued RT and of RT after three WS for both early and on time targets, but not of RT after two WS. It is quite possible that noise and a lack of statistical power limited our capacity to observe a possible relationship between RT and prestimulus activity in the two WS trials, or introduced a random relationship between baseline predictive power and number of WS. However, if the observed pattern of association between prestimulus cerebellar activity and RT observed here is meaningful it may reflect different cerebellar contributions to task performance: a motor preparation component in case the first stimulus is a target and a timing component that acts so as to build up and utilize a representation of the temporal content of the WS. The data presented here suggest

that this “timing” component may not be elaborated fully until the third WS.

The predictive power of baseline cerebellar activity would support the view that cerebellum is involved with the processing of temporal information per se [Ivry and Keele, 1989]. A lack of predictive power for trials with two WS might be interpreted with respect to theoretical considerations of cerebellum as a contributor to adaptive control. Ito [1984, 2005] has suggested that the cerebellum may be considered as a set of microcomplexes that learn to form models of the consequences of signals from other brain areas. Two such models have been proposed: a forward model and an inverse model. A forward model is thought to contribute to error correction for control of movement by providing a prediction for the sensory consequences of motor action. Forward models can also be elaborated for control of cognitive processes. Development of a forward model based on temporal information could act so as to provide a prediction of the timing of future sensory input. Given that two warning stimuli in a single trial unambiguously define a temporal interval, but three are needed to confirm that a prediction for the timing of anticipated stimuli is accurate, the predictive capacity may be fully elaborated only after the third WS has been presented. Kawato et al. [1987] have suggested that at a more advanced stage of learning, an inverse model may be able to take over motor functions entirely, by-passing the motor cortex for over-learned skills. Our finding that motor cortex is predictive of response latency after cueing would be consistent with use of a forward rather than inverse model, although both forward and inverse models may be active during a given cognitive process.

Prestimulus cerebellar activity was a significant predictor of RT for uncued trials and trials with three WS. In each case, the relationship of cerebellar activity to RT was positive: more activity before the beginning of a trial corresponded to slower motor response. If the signal observed from cerebellum reflects Purkinje cell activity that inhibits deep cerebellar nuclei, then lower activity implies disinhibition of the excitatory output to motor structures, which may in turn reflect an earlier start to motor preparation and thus faster RTs. This might be interpretable as an index of efficiency of preparation, or as a somewhat paradoxical index of readiness (i.e., if the cerebellum is active in preparing for perception or response, then it might reduce its activity once preparation is achieved).

The fact that a cingulate source was consistently located in all participants supports previous research implicating this structure in speeded reaction tasks [Naito et al., 2000], although we did not find strong evidence that this structure makes an independent contribution to the prediction of RT. Onset latency of the primary auditory evoked response was not a strong predictor of RT in this study. In contrast, Mäkinen et al. [2004] and Tiitinen et al. [2005] found that peak latency of the auditory evoked response predicted RT, but each of these studies involved stimulus

intensities that smoothly increased from below detection threshold until participants responded that they had detected the stimulus. Smoothly increasing stimulus amplitudes elicited considerable variability in the latency of the primary auditory evoked response. In our paradigm, auditory stimuli were presented at amplitudes well above detection threshold with a brief onset and offset transition. There was little variability in the latency of the sensory cortical response, and hence there was probably a statistical attenuation of the potential correlation between sensory response latency and RT.

CONCLUSIONS

We have observed that temporally structured cueing affects the dynamics of both sensory and motor cortices, allowing faster cortical responses to target stimuli and faster motor responses. This is probably due in part to increasing activation in relevant sensory and motor structures as a result of the WS. In addition, the state of the cerebellum before stimulation partially predicts the speed of response. This may reflect the state of ongoing processes related to attention [Courchesne and Allen, 1997], specifically attention to temporal patterns in presented stimuli [Ivry and Keele, 1989; Tesche and Karhu, 2000], or more generally to the development of predictive models related to the adaptive control of movement [Ito, 2005].

ACKNOWLEDGMENTS

This work was funded by the Mental Illness and Neuroscience Discovery Institute, Albuquerque, NM. Portions of the results were presented as a poster at the 34th Annual Meeting of the Society for Neuroscience, San Diego, CA, 2004. We thank S. Heikkilä and the staff of the BioMag Laboratory for generous assistance in collecting the data.

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