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Nonspatial Saccade-Specific Activation in area LIP of Monkey Parietal Cortex

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Dickinson, A. R., J. L. Calton, and L. H. Snyder. Nonspatial saccade-specific activation in area LIP of monkey parietal cortex. *J Neurophysiol* 90: 2460–2464, 2003. First published June 11, 2003; 10.1152/jn.00788.2002. We present evidence that neurons in the lateral intraparietal area (LIP) of monkey posterior parietal cortex (PPC) are activated by the instruction to make an eye movement, even in the complete absence of a spatial target. This study employed a visually guided motor task that dissociated the type of movement to make (saccade or reach) from the location where the movement was to be made. Using this task, animals were instructed to prepare a specific type of movement prior to knowing the spatial location of the movement target. We found that 25% of the LIP neurons recorded in two animals were activated significantly more by the instruction to prepare a saccade than by the instruction to prepare a reach. This finding indicates that LIP is involved in more than merely spatial attention and provides further evidence for nonspatial effector-specific signal processing in the dorsal stream.

INTRODUCTION

Activity in posterior parietal cortex (PPC) encodes behaviorally relevant spatial information in connection with visually guided movements (Andersen et al. 1985; Kalaska and Crammond 1995; Mountcastle et al. 1975; Platt and Glimcher 1997; Robinson et al. 1978). Lateral intraparietal area (LIP) preferentially encodes targets for upcoming eye movements and de-emphasizes targets for upcoming arm movements (Snyder et al. 1997), a functional specialization that is consistent with the known connectivity of area LIP (Blatt et al. 1990). The reverse pattern is seen in the nearby parietal reach region (PRR), which emphasizes targets for reaches and de-emphasizes targets for saccades (Snyder et al. 1997). Even in the absence of information regarding the spatial goal of the future movement, PRR is preferentially activated by the instruction to prepare a reach, but not by an instruction to prepare a saccade (Calton et al. 2002). Despite these findings, the idea of specialized functions for different PPC regions (Colby 1998) remains controversial, especially with regard to LIP (Bushnell et al. 1981; Gottlieb and Goldberg 1999; Powell and Goldberg 2000). In the current study we asked whether LIP, like PRR, might be differentially activated by a nonspatial instruction to prepare either a reach or a saccade.

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METHODS

Head-fixed animals were trained to make eye or arm movements to spatial targets located 25 cm in front of them on a touch-screen panel. The type of movement (saccade or reach) was instructed using a colored square (effector cue) at the point of fixation (e.g., red signifying saccade, green signifying reach). A blue spot (spatial target) appeared in the periphery to instruct the spatial goal of the movement. These two instructions were provided at two different times, separated by a delay period, and animals were free to initiate the movement as soon as the second instruction had been delivered (cue–delay–target). Eye and arm cue–delay–target trials were randomly interleaved with target–delay–cue trials, in which the instructions were delivered in the reverse order (Fig. 1) (see Calton et al. 2002 for details). LIP was localized to the lateral wall of the intraparietal sulcus where cells showed sustained activity during a memory saccade trial. Cells were selected for analysis on the basis of their showing modulation at any time during a nondelayed reach plus saccade probe task involving movements toward one of eight radial targets equidistant from a central fixation point. For experimental trials, the firing rates were then measured during the delay periods of each task type, between the presentations of the effector cue and spatial target. Typically, spatially targets were presented at one of two locations, either in the preferred direction of the cell or 180° in the opposite direction. Delay period responses were then compared on reach and saccade trials to determine whether LIP was selectively activated by effector information in the absence of a spatial goal.

RESULTS

The activity of 67 LIP cells and 425 non-LIP cells was recorded from the PPC of two male monkeys (*Macaca mulatta*). Effector-specific delay period activity during cue—delay–target trials for a single LIP cell is shown in Fig. 2*A*. There was no transient response to the instructional cues, but following the instruction to prepare a saccade, the cell increased its mean firing rate by 48% from a mean background of 36.2 ± 1.3 sp/s (last 300 ms prior to cue presentation vs. last 300 ms of the delay period; *t*-test, $P < 0.0001$). In contrast, only a small, nonsignificant change in firing was seen following the instruction to prepare an arm movement (16% increase; $P = 0.10$; Fig. 2*A*, dotted trace). The difference between the sustained responses to the two effector instructions was significant (52.8 ± 3.1 vs. 41.9 ± 3.2 sp/s for saccade and reach trials, respectively, last 300 ms of the delay period; $P < 0.05$). Such

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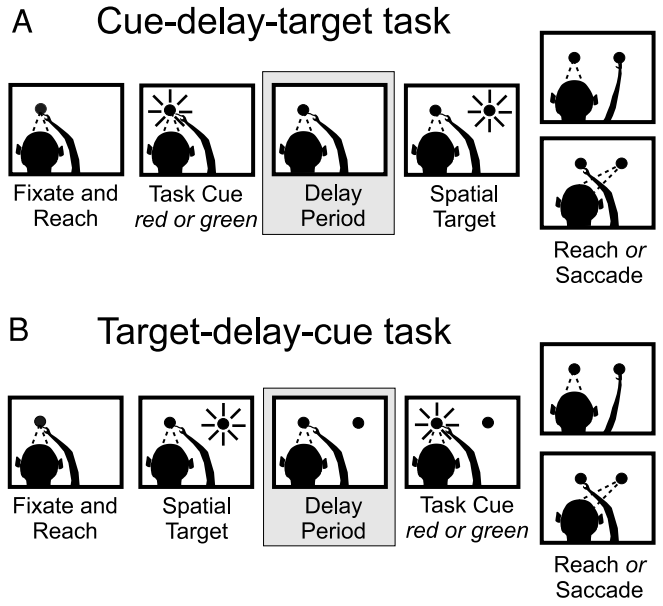

FIG. 1. Task paradigm schematics. Two tasks were interleaved to determine the responses to the independent presentations of effector or spatial target information in LIP. A "cue–delay–target" trial (*A*) began with the monkey fixating both eye and arm on a central visual stimulus projected onto a touch-sensitive screen. After 500–800 ms, the fixation stimulus changed color to instruct either a reach (green) or a saccade (red). A variable delay period (600, 900, or 1200 ms) followed, during which the animal knew what movement to make but not where to make it. All data presented were obtained from the delay period. Finally, a peripheral target appeared, also serving as the "GO" signal for the type of movement previously instructed. In "target—delay–cue" trials (*B*), the stimuli and timing were identical, but the order of presenting effector modality and target location was reversed.

a difference in firing can only have resulted from the distinct effector-specific instructions, since at this time no spatial information had been provided and no movement had begun.

Many LIP cells showed a similar effector-specific increase in sustained activity despite spatial uncertainty. Across the entire population, 25% of the 67 LIP cells were preferentially activated ($P < 0.05$) following the presentation of a cue instructing a saccade compared with a reach. Only 4% showed the reverse preference. An additional 25% of cells showed statistically equivalent increases in firing on both arm trials and eye trials, and 46% were not significantly modulated. Outside of LIP only 7% of cells showed increased activity following a saccade instruction, demonstrating that the increased activation following an eye movement cue seen in LIP was not the result of a change in arousal or some other nonspecific influence.

An effector-specificity index (ESI) was calculated for each LIP neuron using the activity recorded during the last 300 ms of the delay periods in cue–delay–target trials

$$\text{ESI} = (\text{mean firing on eye trials} - \text{arm trials})/(\text{mean firing on eye trials} + \text{arm trials})$$

An absence of effector specificity would result in an ESI of zero. A positive value (max = 1.0) would indicate eye-effector specificity, while a negative value (max = −1.0) would indicate arm-effector specificity. Across the population of 67 LIP cells, ESI values show a small but clear bias in favor of eye-effector specificity (Fig. 2*B*) despite the absence of spatial information. The mean ESI was 0.10, which was significantly different from zero (*t*-test, $P < 0.001$).

Figure 3*A* shows the population-averaged difference in firing evoked by the saccade and reach instructions for all LIP cells (cue–delay–target trials, *bottom trace*). The difference increased steadily from approximately 200 ms after cue presentation until the end of the delay period, with no evidence of an early transient response. Relative to baseline, the mean firing rate across the population increased by 3.1 ± 0.7 sp/s on saccade trials (last 300 ms of delay interval vs. last 300 ms prior to cue presentation; *t*-test, $P < 0.0001$), but only by 1.0 ±0.5 sp/s on reach trials ($P < 0.05$). The difference between saccade and reach trial responses was highly significant ($P < 0.002$). The population data also revealed robust spatial tuning in the absence of an instruction regarding how to use the spatial information (target–delay–cue trials, *top trace*). The appearance of a spatial target evoked a large but transient response, reaching a peak differential (target in the response field minus target outside the field) of 16.5 ± 2.8 sp/s during the interval 160–170 ms after target onset. The differential rate then dropped to an average level of only 4.6 ± 1.1 sp/s, which was sustained to the end of the delay period. The amplitude of the sustained component of this differential response provides a standard against which to compare the response to the effector

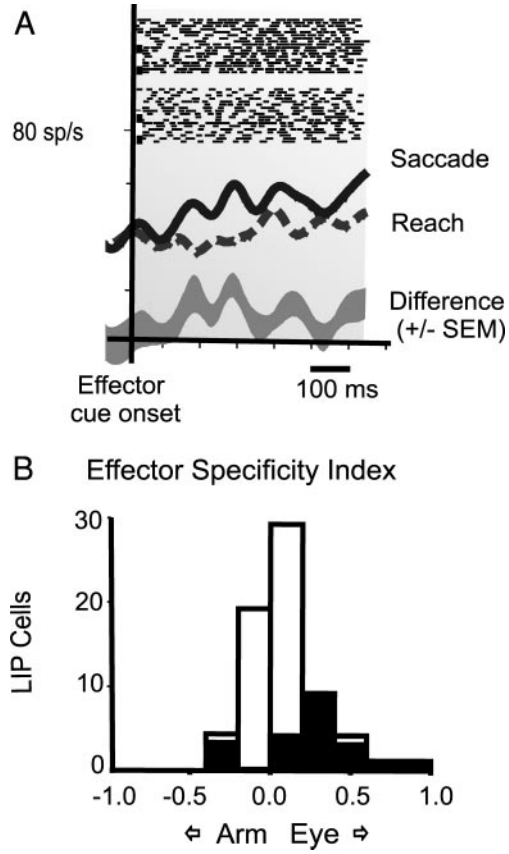

FIG. 2. Effector-specific activation in LIP cells. *A*: for an example cell, in the absence of a spatial target, mean activity increased following a saccade instruction (*top solid trace*) but not a reach instruction (*dotted trace*). Rasters show action potentials across individual trials (upper raster: saccade trials; lower raster: reach trials). The *bottom ribbon trace* shows the mean activity difference ± SE following effector cue. Eighteen reach and 18 saccade trials are shown aligned on the effector cue (vertical line). *B*: over two-thirds of cells show positive effector-specificity index values, indicating robust nonspatial, eye effector-specific activity during the delay period of cue—delay–target trials. Black bars mark significant cells (1-sample *t*-test, mu = 0.00, $P < 0.05$).

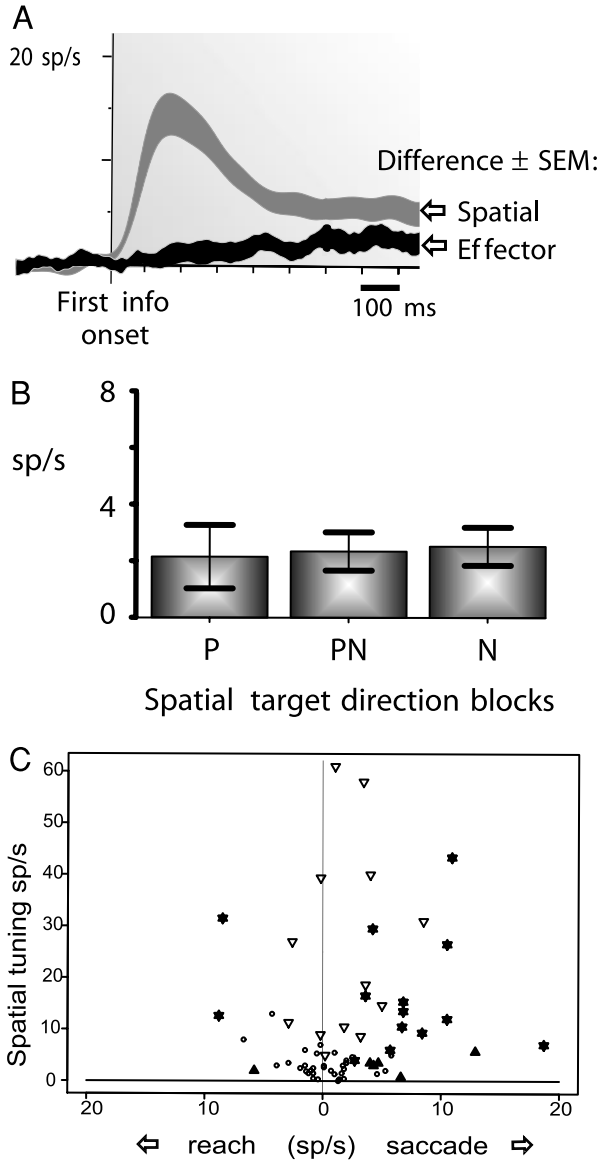

FIG. 3. Effector and spatial activity in LIP cells. *A*: across the population, activity increased more when the animal was instructed to prepare an eye movement compared with a reach movement (*bottom ribbon trace*). The same cells also showed activity differences when the target was presented inside versus outside their receptive fields (*top ribbon trace*). Data are aligned on the first information presented: cue for cue—delay–target trials and target for target–delay–cue. *B*: population-averaged firing differences (eye – arm trials) for 1 versus 2 target direction trial blocks. The same LIP cells ($n = 20$) show similar differential activity across the 3 types of trial block conditions controlling for spatial target prediction (see text for details). P, trials of consecutive preferred direction targets only; PN, interspersed trials of preferred and null direction targets; N, trials of consecutive null direction targets only; histogram shows mean values with SE error bars. *C*: spatial tuning and effector-specific activity occurred independently. Individual cells might show spatial tuning (open inverted triangles), effector-specificity (filled upright triangles), both (stars), or neither (open circles).

cue. In particular, the mean difference in the sustained responses to *nonspatial* effector instructions (reach vs. saccade, cue—delay–target trials, last 300 ms of delay period, 2.1 sp/s) was about half that (45%) of the difference in the sustained responses of the same cells to spatial targets alone (inside vs. outside of the response field, target–delay–cue trials, last 300 ms of the delay period, 4.6 sp/s).

We have asserted that effector-specific responses to the instructional cue occurred independently of spatial information, based on the fact that effector-specific responses occurred prior to the presentation of the spatial cue. However, it is conceivable that the animals guessed where the target might appear and that this prediction provided a spatial substrate on which effector specificity could then operate. Such a prediction could be based on the location of the target on the previous trial. In our data, a target appeared at the opposite (rather than the same) location at a rate slightly above chance (59%, with a SD across data sets of 4%). We tested whether this might influence the effector-specific activity. For each cell, trials were divided into those following a trial in which the target fell in the receptive field (preferred trials) and those following a trial in which the target fell outside the receptive field (null trials). Effector-specific activity was calculated separately for the two conditions. If effector-specific modulation relies on a spatial prediction that is based on the previous trial, then two patterns are possible. If animals predict that targets will recur at the same location as in the previous trial, then effector-specific modulation should occur after preferred but not after null target trials. If animals predict that targets will appear in alternating locations, then effector-specific modulation should occur after null but not after preferred target trials. Instead, we observed that significant effector-specific effects occurred with nearly equal probability regardless of whether a preferred (7 of 67 cells) or null (6 cells) target had appeared on the previous trial. There was similarly no evidence for a dependence of effector-specific activity on whether the previous trial instructed the use of the same or a different effector. Effector-specific responses thus correlated with neither the target location nor the effector of the previous trial.

A related possibility is that the mere chance of having a target land in the receptive field provides a predictive spatial signal on every trial, with a magnitude inversely proportional to the number of targets being used. Such an effect has been reported in the superior colliculus (Basso and Wurtz 1998), though it was shown not to play a role in effector-specific activity in PRR (Calton et al. 2002). To explicitly test this hypothesis in LIP, we identified an additional 43 LIP cells from which a subset of 20 showed a clear eye-effector preference. We recorded from each of these 20 cells in blocks of trials within which either one target or two interspersed targets were presented. First, 40 trials of interspersed eye and arm trials were obtained using interspersed null and preferred targets. Next, two 20-trial single target blocks were collected, one using only preferred targets and one using only null targets. The spatial prediction hypothesis would predict that there should be maximal activity prior to target appearance on preferred blocks, no activity on null blocks, and intermediate activity on two target blocks. Instead, we found little or no effect of this manipulation on effector-specific activity prior to the presentation of a spatial target (Fig. 3*B*). The population-averaged firing differences between eye and arm trials were not significantly different between the three conditions (preferred vs. 2-directions; null vs. 2-directions; preferred vs. null direction; $P > 0.8$, 2-tailed *t*-test for all three comparisons). The mean differential firing rates for interspersed preferred and null direction target trials (2.34 ± 0.68 sp/s) and the mean differential rates for null target trials alone (2.52 ± 0.67) were both significantly greater than zero ($P < 0.01$, 1-tailed *t*-test). The

mean differential rates for preferred target trials alone (2.15 ± 1.12) showed a similar trend ($P < 0.1$). These data indicate that effector specificity was largely independent of spatial target direction and predictability. For this analysis, the first 8 trials of each block were excluded. Similar findings were obtained when different numbers of initial trials were excluded.

We believe that our block size of 20 to 40 trials was long enough for animals to adjust their spatial predictions to the particular pattern of target locations. To test this, we compared saccadic and arm movement reaction times in one and two target blocks. Arm reaction times were significantly faster when a single target versus double target condition was presented (225.5 ± 1.1 vs. 229.4 ± 1.4 ms, 1-tailed *t*-test, $P < 0.01$). We failed to find a similar effect in our eye movement data (140.8 ± 0.7 vs. 136.2 ± 0.8 ms, $P > 0.5$). However, since several previous studies either have failed to find a drop in saccade latency with fewer targets (Kveraga et al. 2002) or have not reported the data (Basso and Wurtz 1998), we conclude that the observed drop in arm movement latency with fewer targets is sufficient to indicate that our animals adjusted their spatial predictions across blocks.

It is possible that spatial and effector signals are segregated at the level of LIP and then are combined only at a later stage of processing. Alternatively, the combination of these two signals could occur within LIP. We have found the latter to be the case. Figure 3*C* plots the difference in firing due to spatial tuning in the absence of effector information (target–delay–cue trials, target inside minus outside the receptive field of the cell) as a function of the difference in response due to effector specificity in the absence of spatial information (cue—delay–target trials, saccade minus reach). It is clear that the effector-specific and spatially responsive cells do not comprise mutually exclusive subpopulations of LIP cells, nor do they comprise a single cell population, as might have been expected if (predictive) spatial signals were required for the expression of effector specificity. Eighteen percent of cells showed spatial tuning (50–150 ms after the target appearance) but no lacked effector specificity (hollow triangles), 9% showed only significant effector specificity (last 300 ms of delay period after the cue had appeared) but insignificant spatial tuning (filled triangles), and 21% showed both effects (stars). Across the entire population, there was no significant correlation between effector specificity and spatial tuning (correlation coefficient, $r = 0.13$, $P > 0.1$).

DISCUSSION

Effector-selective LIP activity in the presence of both spatial and effector information was previously demonstrated by Snyder et al. (1997). We now show that LIP can be activated by effector information alone, simply by cueing an eye movement in the complete absence of a spatial target. This finding is consistent with a role for LIP in the preparation (though not necessarily the generation) of eye movements toward upcoming targets and is consistent with the more general view of Goodale and Milner (1992) that the dorsal stream has evolved to support visually guided action.

Our results challenge the view that PPC is dedicated solely to representing salient spatial locations (e.g., Goldberg et al. 2002). One way to reconcile the current findings with a purely attentional view of the PPC is to hypothesize that preparing to move the eyes results in a heightened state of attention compared with preparing to move the arm. This attempt at reconciliation fails, however, since PRR shows the reverse pattern of effector-specific activation (Calton et al. 2002). In our view, attention is necessarily generic, so that the notion of effector-specific attention is tautological. This is not to say that LIP activity is completely independent of attention. If fact, the current results show that LIP can be activated by spatial information prior to receipt of an instruction regarding how that spatial information is to be used (target–delay–cue trials). Indeed, the sustained response to pure spatial information is about twice as large as the sustained response to pure effector information. Interestingly, this ratio is similar to that found in PRR, suggesting that analogous architectures might underlie the combining of spatial and effector-specific information in these two areas. In LIP and, to a lesser extent, in PRR, the appearance of a spatial target produces a very large transient response. An unresolved issue is whether the large responses to pure spatial information in LIP and PRR are best thought of as attentional modulations or rather as default plans for an eye and an arm movement, respectively.

This study has determined the encoding of nonspatial, effector-specific movement instructions (motor-specific intention) to be a characteristic of LIP cells. We conclude that the dorsal stream combines distinct forms of effector-specific intention with visuospatial target information, within the same cells, and in multiple areas within PPC (reach preparation in PRR, saccade preparation in LIP).

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DISCLOSURES

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