NeuroImage 87 (2014) 476–489

Contents lists available at ScienceDirect

NeuroImage

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

Two-dimensional spatial tuning for saccades in human parieto-frontal cortex

Frank T.M. Leoné *, Ivan Toni, W. Pieter Medendorp

Radboud University Nijmegen, Donders Institute for Brain, Cognition and Behavior, 6525 HR Nijmegen, The Netherlands

ARTICLE INFO

Article history:
Accepted 26 September 2013
Available online 4 October 2013

Keywords:
Topography
Saccade amplitude
Frontal eye fields
Intraparietal sulcus
Singular value decomposition

ABSTRACT

Saccades in the frontoparallel plane are targeted at two-dimensional (2D) locations, defined by direction and amplitude. Macaque neurophysiology has shown that these dimensions are jointly represented in single intraparietal sulcus (IPS) and frontal eye fields (FEF) neurons, constituting multiple maps of 2D saccade space. Human fMRI has shown that the direction of the saccade is topographically represented across large neuronal groups. However, it is unknown whether both direction and amplitude are separable dimensions at the voxel level and whether these tuning variables are organized in large-scale topographic maps. We used fMRI to address these issues in subjects performing an instructed-delay saccade task to 18 locations (6 directions, 3 amplitudes). Singular value decomposition was applied to the corresponding response field of each voxel, providing an index of the separability into direction and amplitude tuning. Our findings show that saccade location tuning is composed of separable direction and amplitude components within voxels across the parieto-frontal network. In both IPS and FEF there were amplitude gradients and reversals of direction tuning across voxels, with a medio-lateral gradient of decreasing saccade amplitude along the IPS. These findings reveal the 2D cortical organization of saccade space within and across voxels and hold great potential for the study of other sensorimotor systems.

Introduction

Various regions in the primate neocortex have been implicated in generating saccades, including key areas such as the lateral intraparietal area (LIP) and frontal eye fields (FEF) (see Munoz and Everling, 2004 for review). These regions need to code two dimensions to program saccades in the frontoparallel plane: target direction and target amplitude. Single-unit electrophysiology in macaques has shown that these parameters are jointly represented in individual neurons, resulting in two-dimensional (2D) tuning curves (Bruce and Goldberg, 1985; Bruce et al., 1985; Gnadt and Breznen, 1996; Goldberg and Bruce, 1990; Platt and Glimcher, 1998). Furthermore, in areas LIP and FEF, adjacent neurons show similar tuning properties, resulting in topographic maps of saccade space (Gnadt and Andersen, 1988; Goldberg and Bruce, 1990; Thier and Andersen, 1998). However, it is unknown to what extent 2D tuning and topography generalize to computations of larger neuronal pools, like those sampled in fMRI voxels, and to other species, including humans.

In human saccade planning, several fMRI studies have applied phase-encoded mapping approaches to map one of the two dimensions – target direction – along the parieto-frontal surface. This approach has identified up to seven regions with directional topography in parietal cortex and two such regions in frontal cortex (see Silver and Kastner, 2009 for review). To date, however, no reports exist on the cortical representation of saccade amplitude in humans.

In close connection, studies of visual perception have reported 2D visuotopic maps in occipital and parietal areas, based on responses to rotating wedges and moving ring stimuli (Arcaro et al., 2011; Swisher et al., 2007). The visual stimulation in such studies is varied along one dimension only (e.g., a concentric ring), mapping direction and amplitude independently. It is not clear whether these results generalize to saccades, which would require that direction and amplitude are separate, independent dimensions in 2D saccade tuning. In principle, this means that the shape of the tuning curve for direction does not depend on amplitude, and vice versa. However, this has never been tested in humans.

Hence, the current knowledge on human cortical 2D saccade generation leaves open two important questions. How are saccade locations represented at the level of individual voxels, i.e., as a combination of direction and amplitude? How are saccade locations topographically represented across the parieto-frontal cortex?

To answer these questions, we measured cerebral activity with fMRI while participants performed saccades to remembered visual targets, presented at 18 different locations in the fronto-parallel plane. Inspired by analyses of single-unit data in owls (Peña and Konishi, 2001) and macaques (Pesaran et al., 2006), we used singular value decomposition (SVD) on BOLD timeseries to study saccade organization at two levels. First, we applied SVD at each voxel to test the separability of location-related responses in direction and amplitude components. Second, taking the voxels of which the location response proved separable, we used the peak of the direction and amplitude components to determine the full 2D topography for saccades across voxels. Differently from previous work, these novel analyses derive direction and amplitude tuning from location

* Corresponding author.
E-mail address: f.leone@donders.ru.nl (F.T.M. Leoné).

1053-8119/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2013.09.067

data, testing whether these dimensions are cerebrally relevant for representing saccade locations.

Materials and methods

Participants

Eight healthy right-handed participants (five male, three female), average age 24.6 (range 19–43 years), with normal or corrected to normal vision, participated in this study. A short questionnaire was used to assess handedness. Each subject participated in two recording sessions of about 60 min each, performing a total of 1296 saccade trials Participants gave their written consent in accordance with the local ethics committee (CMO Committee on Research Involving Human Subjects, region Arnhem–Nijmegen, The Netherlands).

Experimental set-up

Participants were lying supine in the scanner; their head was tied inside a phased-array receiver head coil. The head and neck were stabilized within the head coil using foam blocks and wedges. A foam block was also placed underneath the knees. In some subjects the elbows and neck were further supported by cushions to make them feel more comfortable. Visual stimuli were projected onto a screen and viewed by the subject using a mirror, giving the perception that they were roughly above the participants' head. Stimuli were controlled using Presentation software (Version 14.7; Neurobehavioral Systems, San Francisco, CA, USA). Position of the left eye was recorded using a long-range infrared video-based eyetracker (SMI, Teltow, Germany) at a frequency of 50 Hz.

MRI settings

MR images were acquired using a Siemens Trio 3-Tesla MRI scanner (Siemens Tim TRIO, Erlangen, Germany) with a 32 channel head coil. A multi-echo sequence of five echoes (TE: 9.4, 21.2, 33, 45, 57 ms, TR: 1480 ms) was used to improve signal strength, encompassing 23 slices, centered on the parietal and frontal motor areas (slice thickness 3 mm, gap = 17%, in-plane pixel size 3 × 3 mm, FOV 192 mm, flip angle = 80°). 210 functional images were obtained per run, lasting 5 min, with 24 runs in three subjects, and 28 runs in one (S1). After collecting the functional images, high-resolution anatomical images were acquired using a T1-weighted MP-RAGE GRAPPA sequence (176 sagittal slices, voxel size = 1 × 1 × 1 mm, TR = 2300 ms, TE = 3.93 ms, FOV = 256 mm, flip angle = 8°).

Experimental paradigm

We designed our experimental paradigm with a clear connection to previous paradigms, facilitating a comparison to established topographic mapping approaches and their respective results. To this end, our subjects performed a memory-guided saccade task (see Fig. 1A), with the target location successively stepping through 60° angular intervals around the clock (30 ("1 o'clock"), 90, 150, 210, 270, 330°) followed by an eccentricity (amplitude) change (4, 8 or 12°) after each full round of fixations (see Fig. 1B). Each trial started with the presentation of the peripheral target (a white dot, size: 1°) for 500 ms, while subjects fixated a central white cross (size: 1°). Subsequently, a set of 500 dots (size: 1°), equally distributed across the field of view blinked at 2 Hz for 3 s, removing iconic memory traces (Averbach and Coriell, 1961). The subject was instructed to plan a saccade movement to the remembered target during this period. Next, the fixation cross dimmed for 750 ms. This instructed the subject to execute the planned saccade to the remembered target location and immediately return to the central fixation cross. The next trial started after the central fixation cross was presented at normal luminance for a duration of 750 ms. Each trial lasted 5 s. Trial length was not jittered to allow for phase-based analysis approaches (Schluppeck et al., 2005; Sereno et al., 1995). The 60° steps in target direction across subsequent trials occurred in either clockwise or counterclockwise direction. The 4° steps in target amplitude were superimposed on direction changes, either away from or towards the fixation cross. As a result, the successive presentation of the 18 target locations was either in a clockwise-inward, counterclockwise-inward, clockwise-outward, or a counterclockwise-outward fashion. A sequence was repeated three times within a run, yielding a total of 54 trials per run. Each run was preceded and followed by 20 s of steady gaze fixation. Runs were separated by breaks during which the scanner was turned off and the lights were turned on. The duration of the breaks was determined by the subject. The total duration of the experiment, consisting of 24 runs or 1296 trials, excluding the breaks, was 124 min, performed in

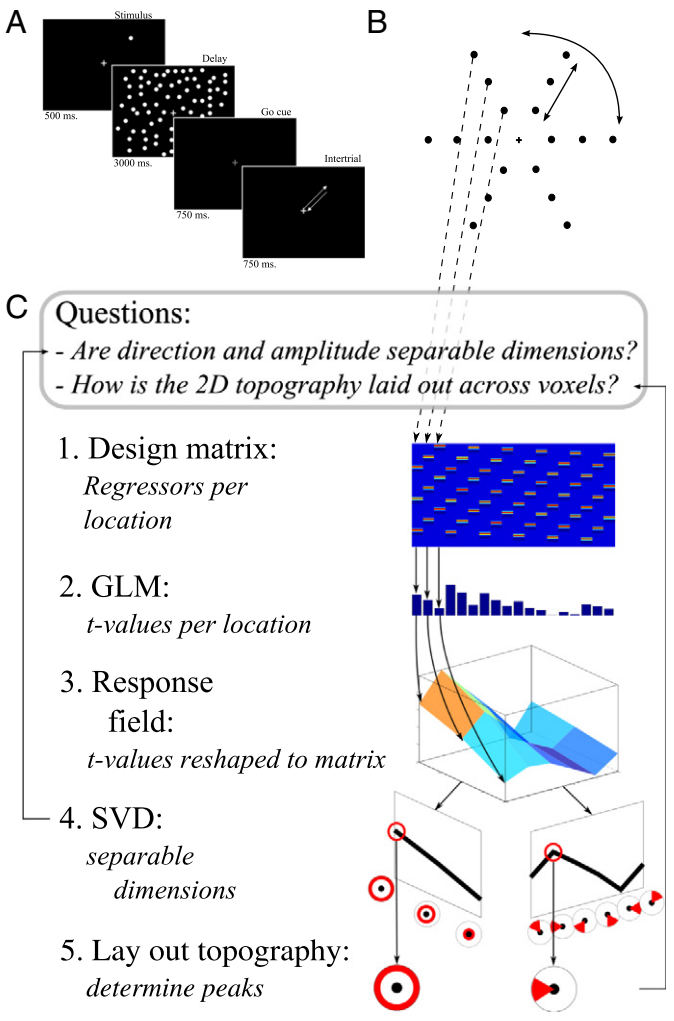

Fig. 1. Experimental paradigm and analysis (A). Each trial started with the presentation of the stimulus (500 ms) at one of 18 target locations. This was followed by 3 s of distractor flashes, after which participants made the movement to the remembered target and back, as triggered by the movement cue (750 ms). A trial ended with 750 ms of only the fixation cross, after which the next trial followed. (B) The 18 possible saccade target locations as presented in the stimulus phase. Solid arrows indicate the two axes on which the order of saccade target presentation could differ between runs: direction (leftward or rightward) and amplitude (inward or outward). (C). Overview of analysis. 1. A design matrix was constructed containing, among others, 18 regressors of interest capturing the planning periods, one for each of the 18 saccade target locations. 2. A standard GLM analysis was used to calculated t-values (indicated by blue bars) for each regressor per voxel. 3. The t-values were ordered in a 3 × 6 matrix to mimic the underlying spatial structure of the stimuli and form a response field (indicated by the surface plot, the arrows how the t-values and respond field relate). 4. SVD was applied to extract the primary direction and amplitude dimensions of the response field (amplitude is indicated using red rings, direction by red wedges). 5. Topography was laid out across voxels by determining the peak of tuning (indicated by arrow and red circle) along the separated dimensions. The results of the SVD and determination of peaks relate directly to our two research questions.