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Multisensory Representations of Space: Multimodal Brain Imaging Approaches

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy

in
Cognitive Science

by
Ruey-Song Huang

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2006
The dissertation of Ruey-Song Huang is approved, and it is acceptable in quality and form for publication on microfilm.

Chair

University of California, San Diego

2006
Dedicated to
my parents

and

my advisors

Drs. Marty Sereno and Tzyy-Ping Jung
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\textbf{FIELDS OF STUDY}

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Studies in EEG Brain Dynamics
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Humans and other primates evolved and live in a three-dimensional space. How and where spatial information is represented in the brain is an important issue in cognitive neuroscience. Evidence from monkey neurophysiological studies suggests that several cortical areas encode spatial information in various reference frames, such as eye-centered, head-centered, arm-centered, object-centered, and body-centered coordinates. Some areas may combine information across multiple sensory modalities to form a coherent representation of the world.

Topographic mapping is a fundamental organizing principle of sensory systems. Several retinotopic (eye-centered) maps have been revealed by functional magnetic resonance imaging (fMRI) in humans. It is not clear, however, whether other spatial reference frames are also represented as continuous topographic maps on the cortical surface. The goal of this dissertation is to investigate cortical representations of multiple reference frames across multiple sensory modalities using multiple brain imaging techniques.
The first study uses fMRI to investigate higher-level retinotopic maps with wide-field phase-encoded video stimuli. Results showed that retinotopy extended anteriorly along the fusiform gyrus in the ventral surface, beyond MT+ into the superior temporal and lateral sulci, beyond LIP+ into postcentral sulcus, and medially into posterior cingulate cortex.

The second study investigates cortical representations of skin surface using an MR-compatible somatosensory stimulation system and phase-encoded methods. Multiple somatotopic representations of the face, lips, and fingers were mapped in primary motor cortex (MI), ventral premotor cortex (PMv), polymodal zone (PZ), primary (SI) and secondary (SII) somatosensory cortex, parietal ventral area (PV) and 7b, as well as anterior and ventral intraparietal areas (AIP and VIP).

The third study investigates a multisensory parietal face area revealed by both of the previous studies. This area is considered a human homologue to area VIP in the macaque, which contains aligned head-centered visual and tactile maps. A surface coil was constructed to obtain high-resolution mapping in this area. Cognitive functions and multisensory interactions in this area were investigated in several paradigms, including structured motion, phase-encoded looming objects, imagination of navigation, and multisensory random block designs.
Chapter 1

Retinotopy of Human Cortex Using Wide-field Phase-encoded Video
Abstract

Phase-encoded retinotopic mapping experiments using flickering checkerboards were less effective for mapping higher level visual areas activated in cognitive difference paradigms designed to localize complex object recognition, structural motion, spatial attention, and saccade eye movements. The goal of this study was to derive high-resolution maps of other higher-level visual areas by using more naturalistic stimuli. Subjects viewed videos of television programs presented through moving retinotopic masks with a central fixation. Their task was to summarize the plot afterwards. Wide-field phase-encoded video stimuli retinotopically activated a number of more anterior cortical areas beyond well-defined retinotopic maps in occipital cortex. Retinotopy extended anteriorly along the fusiform gyrus in the ventral surface, beyond MT+ into the superior temporal sulcus and lateral sulcus, beyond LIP+ into the postcentral sulcus, and medially into the posterior cingulate cortex. Several retinotopic maps, including VIP+, LIP+, MT+ (MT, MST, FST, V4t), PreC, V6, hV4, V8/VO-1, VO-2, were defined in this study.

Introduction

Several dozen visual areas have been described so far in non-human primates (Felleman and Van Essen 1991; Kaas and Krubitzer, 1991; Sereno and Allman, 1991; Lewis and Van Essen 2000a, 2000b; Gattass et al., 2005). Using various neuroimaging methods, several of these areas have been mapped in humans (Watson
et al., 1993; Engel et al., 1994, 1997; Sereno et al., 1995; Tootell et al., 1995, 1996, 1997, 1998a, 1998b, 1998c; De Yoe et al., 1994, 1996; McKeefry and Zeki, 1997; Tootell and Hadjikhani, 2001). In particular, areas V1, V2, V3, VP, V3A, V4v, and MT/V5 have been named in humans based on homologies with non-human primate areas (see reviews in Sereno, 1998; Tootell et al., 2003; Orban et al., 2004; Van Essen, 2004; Rosa and Tweedale, 2005; Sereno and Tootell, 2005).

Retinotopic mapping using phase-encoded stimuli, such as flickering checkerboards contained in a rotating wedge or in an expanding/contracting ring, has successfully revealed maps in the aforementioned areas in human fMRI experiments. However, the flickering checkerboard stimuli seem to be less effective for retinotopic mapping beyond early visual areas (Sereno et al., 1995; Tootell et al., 1998c, Wandell, 1999; Dougherty et al., 2003; Slotnick and Yantis, 2003; Warnking et al., 2002; Wandell et al., 2005).

Several possibilities may account for the unsuccessful search for retinotopic maps in high-level visual areas. First, single-cell recording in monkeys provides less evidence for topographic maps in higher areas (Felleman and Van Essen 1991; Sereno and Allman, 1991), and it was inferred that the same is true for humans. Second, during the early stage of fMRI development, the coverage of total brain regions in a single functional scan may have been constrained by available imaging techniques, e.g., the pulse sequences were not fast enough to cover enough slices beyond visual cortex. Third, the signal-to-noise ratio (SNR) in lower field scanners (e.g. 1.5 Tesla) was not high enough. Surface coils were placed near the regions of interest, such as the occipital cortex, in order to achieve maximum SNR. The rapid
fall-off away from the site of the surface coil would have reduced the likelihood of detecting of new maps even if they existed (Sereno et al., 1995). Fourth, the flickering-checkerboard paradigms required that subjects maintain central fixation and watch the stimuli passively. The checkerboard stimuli may not activate higher visual areas that prefer complex visual patterns. Fifth, the visual stimuli in most retinotopic studies often extended to less than 20 degrees in eccentricity. These limitations may constrain the retinotopic maps to the central vision in the ventral stream of visual cortex (Baizer et al., 1991). The dorsal stream, also know as the “where” pathway is important for spatial attention and prefers stimuli in the periphery (Ungerleider and Mishkin, 1982).

Studies using complex natural stimuli, such as objects, faces, body parts, point-light biological motion, and videos, have shown visually-driven activities in brain regions beyond early visual areas (Kanwisher et al., 1997; Halgren et al., 1999; Grossman et al., 2000; Levy et al., 2001, 2004; Malach et al., 2002; Grossman and Blake, 2002; Hasson et al., 2002, 2004; Avidan et al., 2003; Beauchamp et al., 2003; Bartels and Zeki, 2004, 2005; Saygin et al., 2004; Wheaton et al., 2004). Higher level areas can also be driven by attention (Simon et al., 2002; Astafiev et al., 2003). It is not clear, however, whether higher visual areas are also organized into retinotopic maps. Recent studies have suggested that retinotopic maps exist in premotor and prefrontal cortex (Hagler and Sereno, 2006), posterior parietal cortex (Sereno et al., 2001, 2003, 2004; Schluppeck et al., 2005, 2006; Silver et al., 2005), and the highest level of association cortex in the superior part of the postcentral sulcus (Huang and Sereno, 2005; Sereno and Huang, 2006).
In this study, close-up wide-field phase-encoded stimuli containing natural video were used to reveal retinotopic maps in higher order visual areas. Compared to checkerboards, the videos attract more attention, have spatiotemporal statistics closer to real world stimulation, and have been found to activate strongly both lower and higher visual areas in humans (Sereno et al., 2003, 2004). Several retinotopic maps were revealed in the superior parietal, posterior parietal, medial parietal, ventral occipital, lateral occipital, and middle temporal cortex.

Materials and Methods

Subjects

24 healthy subjects (11 males, 13 females; aged 20-50) with (or corrected to) normal vision participated in this study. Each subject participated in at least two fMRI sessions. Subjects gave informed consent, according to protocols approved by the Human Research Protections Program of the University of California, San Diego.

Experimental paradigms and visual stimuli

Subjects were scanned as they watched naturalistic videos (e.g., episodes of the television action program, “Xena: Warrior Princess”) in three paradigms: video ON vs. OFF, video masked inside a rotating wedge, and video masked inside a contracting or expanding ring. The video stimuli were generated by in-house OpenGL programs (by M.I.S.) on an SGI O2 workstation that took NTSC input frame in real-time. Video frames were scaled and centered within the apertures (circle, wedge,
and ring) before the moving mask was drawn on top of each video frame. Subjects were required to fixate the central cross, attend to the videos, and attempt to follow the story during the functional scans. The stability of fixation was verified by tests with a pupillometer outside the scanner. Subjects listened (through ear plugs) to the stereo soundtrack of the video via MR-compatible headphones (Resonance Technology, Northridge, CA) during the entire fMRI session.

The first block-design paradigm was used to outline the entire extent of visually-driven cortex (Hasson et al., 2004). Subjects watched video presented in a full-screen circular mask (Fig. 1.1A) while fixating a central cross for 16 seconds (ON-block), and remained fixating the central cross against a black background for 16 seconds (OFF-block). The soundtrack was audible during the entire scan (16 cycles/512 seconds).

The second phase-encoded paradigm was used for mapping representations of visual field polar angle. The stimuli were similar to those previously used for retinotopic mapping (Sereno et al., 1995), but the flickering checkerboard in the rotating wedge was replaced with video. A black mask containing a 45-degree-wide wedge-shaped aperture was drawn on top of the video (Fig. 1.1B). Each video frame was scaled down to the approximate size of the aperture and then translated so that the center of each frame always appeared at the center of the wedge, which slowly and smoothly rotated around a central fixation cross (64 sec/cycle, 8 cycles/scan). In a 512-s scan, subjects viewed polar angle stimuli rotating in either clockwise or counterclockwise directions; two scans were conducted for each direction.

The third phase-encoded paradigm was used for mapping representations of
eccentricity of the visual field. A black mask containing a ring-shaped aperture was drawn on top of the video (Fig. 1.1C). Each video frame was scaled down to the approximate size of the aperture, which slowly and smoothly expanded or contracted logarithmically around a central fixation cross (64 sec/cycle, 8 cycles/scan). Subjects viewed expanding and contracting stimuli in two 512-s scans, respectively.

**Experimental setup**

A semicircular back-projection Plexiglas screen was designed (by R.-S.H.) to take up the entire space between the ceiling of the scanner bore and the subject’s chest. Subjects were instructed to attach the screen to the ceiling with Velcro after they were placed at the iso-center of the magnet. Subjects adjusted the screen at a distance 10 to 15 cm in front of their eyes so that they could comfortably fixate and focus on a red cross on the screen without blurring. Stimuli were projected onto the screen at full extent using an XGA video projector (NEC, Japan; 1024x768, 72 Hz, 10-20 pixels per degree of visual angle) whose standard lens had been replaced with a 7.38 – 12.3” focal length XtraBright zoom lens (Buhl Optical, USA) in order to achieve high-resolution images on the screen inside the bore (a distance of 3-4 meters). Subjects lay on the scanner bed with their heads tilted forward (~ 30 degrees) so that they could view the stimuli on the screen directly without a mirror. A bite bar was not used because its arm would block the stimuli. Instead, foam padding was inserted in the head coil to minimize head movement and support the tilted head.

The direct-view setup is critical because the visible area is limited when a
mirror is used. Even if the stimuli were projected on a large screen, the longer eye-to-screen distance would reduce the visual angle of the stimuli. The direct-view setup also prevented the subjects from seeing two copies of the stimuli, directly from the screen and indirectly through the mirror. It is also difficult to eliminate all direct-view stimuli when a mirror is used especially at larger eccentricities. The ergonomics of our stimuli presentation greatly increased the size of the visual field that was stimulated; polar angle and eccentricity visual stimuli subtended up to 100 (± 50) degrees horizontally, 80 (± 40) degrees vertically in the visual field. Brain mapping studies on the human visual system have typically used much smaller visual stimuli (8 to 12 degrees eccentricity from the fixation point); consequently, these stimuli do not directly activate the periphery in many cortical visual areas (e.g., Sereno et al., 1995; Tootell et al., 1997, 1998; Brewer et al., 2005; Wandell et al., 2005).

The very large stimuli used here also help to deal with a possible confound in fMRI mapping studies due to surround inhibition. fMRI studies in non-human primates studies suggest that when a local area of visual cortex is stimulated, surrounding areas of a cortical visual map that have not been directly stimulated show both a reduction in single unit activity as well as a reduced BOLD fMRI signal (Chen et al., 2005). In phase-encoded retinotopic mapping studies, cortical map regions that are never directly activated by the retina, but which are near periodically activated regions -- e.g., retinotopic cortical map representations of visual space just beyond the peripheral edge of a rotating wedge -- will therefore also generate a periodic signal. However, this signal will have a phase offset of 180 degrees from
the veridical phase of the periodic signal in the nearby retinally stimulated region because the BOLD signal in these regions would be reduced every time the stimulus sweeps by. By stimulating most of the visual field, this misleading signal -- that is, misleading for the purposes of retinotopic mapping -- is greatly reduced (Sereno and Tootell, 2005; Pitzalis et al., 2006).

**Imaging parameters and data analysis**

Echo-planar images were collected during 512-s runs (3T GE Signa Excite, 8-element phased-array head coil, single shot EPI, 3.125x3.125 mm in-plane, 3-4 mm thick slices, 256 images per slice, 31 axial slices, flip angle = 90 deg, TE = 30 ms, TR = 2000 ms, 64x64 matrix, bandwidth = 1800 Hz/pixel). A total of 168 functional scans were performed on 24 subjects, including 7 functional scans per subject. Functional scans were motion-corrected using AFNI 3dvolreg. FreeSurfer (Dale et al., 1999) was used to reconstruct the cortical surface for each person from a pair of registered structural scans (FSPGR, 1x1x1 mm) taken in a separate session. The last scan of each functional session was an alignment scan (also FSPGR, 1x1x1.3 mm) acquired in the plane of the functional scans and used to establish an initial registration of the functional data with the surface, which was then refined using manual blink comparison with the structural images to achieve an exact overlay of the functional data onto each cortical surface. To increase SNR, we typically combined four 512-s scans for each task. To determine which areas were significantly activated as well as the phase of that activation, a Fourier transform was computed for the time series at each voxel after removing the linear trend. An F-ratio was constructed by
comparing the power of the (complex) signal at the stimulus frequency (8 or 16 cycles per scan) to the power of the noise (other frequencies). Very low frequencies (movement artifact) and harmonics were excluded. The F-ratio was then converted to a (uncorrected) p-value by considering degrees of freedom of the signal and noise. In two-condition experiments, the phase angle at the stimulus frequency was divided into two bins corresponding to responses to ON and OFF blocks, and the ON phases displayed using a heat scale ending in white (OFF block responses were negligible in all four two-condition experiments). In mapping experiments, the phase angle was displayed using a continuous color scale (red → blue → green). In both cases, the saturation of the colors was modulated by the p-value, as illustrated in the color bar insets in the Figures. The software used for data analysis is available for free download (binaries for IRIX and Linux) at http://surfer.nmr.mgh.harvard.edu/download.html. A download that also includes retinotopy analysis tools is available at http://kamares.ucsd.edu/~sereno/csurf/tarballs/.

**Group average**

To average mapping data across subjects, we used a new method for group analysis of phase-encoded retinotopic mapping data developed in our lab (Hagler and Sereno, 2006). The individual unfolded cortical surfaces were first inflated to a sphere, and then non-linearly morphed into alignment with a canonical target sphere brain (icosahedral supertessellation) by minimizing local differences in average convexity (“sulcus-ness”; see eq. 9, Fischl et al., 1999a) while minimizing metric distortion.
Complex-valued single-subject mapping data (amplitude and phase of significant periodic responses) were averaged across subjects by vector addition at each vertex of the canonical spherical surface. As with vector averaging of clockwise-counterclockwise data, this procedure strongly penalizes surface locations with inconsistent phase across subjects, even if those locations are significantly activated in each subject. The average map was then resampled back onto an individual brain for display. This averaging procedure was justified by the fact that surface-based morphing does a good job of aligning independently obtained retinotopic maps (Fischl et al., 1999b).

**Results**

To validate retinotopic mapping using phase-encoded video stimuli and to compare with studies using flickering checkerboards, maps of polar angle, eccentricity, and field sign of a representative subject were rendered on flattened cortical surfaces as shown in Fig. 1.2. Early visual areas, including V1, V2, V3, V3A, V7, VP and V4v and the borders between these areas agree with retinotopic maps defined in previous studies (Sereno et al., 1995; Tootell et al., 1996, 1997, 1998a, 1998b, 1998c). Three additional areas, V6, V8 and MT (middle temporal), also showed a complete representation of the contralateral hemifield in the polar angle maps. Area MT showed clear representation of the center of gaze inferior to the representation of peripheral visual field in the eccentricity maps (Huk et al., 2002).

Areas activated by video (ON-block) in the first block-design paradigm were
rendered on inflated cortical surfaces of a second subject as shown in Fig. 1.3. Starting from the occipital pole, visually-driven areas extended anteriorly along the fusiform gyrus in the ventral surface, beyond area MT/V5 into the superior temporal sulcus and lateral sulcus, anteriorly into the postcentral sulcus in the parietal cortex, and medially into posterior cingulate cortex. The video stimuli also activated two additional areas, frontal eye fields (FEF) and ventral premotor (PMv), anterior to the central sulcus (Saygin et al., 2004; Hagler and Sereno, 2006).

The second and third phase-encoded paradigms further revealed several clusters of retinotopic areas also activated by the first paradigm, including ventral intraparietal areas (VIP+), middle temporal areas (MT+), lateral intraparietal areas (LIP+), precuneus (PreC), and area V6, as circled in Fig. 1.4. Each of these areas will be discussed in details with close-up maps (as outlined by the white squares in Fig. 1.4) from several representative subjects.

**Anterior and Superior parietal areas (VIP+)**

Fig. 1.5 shows a dorsal lateral view of six unfolded hemispheres of single-subject data and both hemispheres of the 24-subject-average data. An area located at the confluence of the postcentral and intraparietal sulci in the superior parietal lobe contains a complete representation of the contralateral visual hemifield. In general, the upper visual field representation (red) is located medial and anterior to the lower field representation (green), as shown in single-subject and 24-subject-average data. This area responds to multisensory (visual, tactile, and auditory) stimuli, contains aligned maps of tactile and near-face visual stimuli.
(Huang and Sereno, 2005; Sereno and Huang, 2006), and may be considered the human homologue of area VIP (ventral intraparietal sulcus) in the macaque monkey. In addition, this area may contain more than one part even in macaque monkeys (Lewis and Van Essen 2000a, 2000b; Gattass et al., 2005) and is tentatively labeled as human VIP+ (the “+” sign indicates multiple subdivisions).

In some subjects, an area in the postcentral sulcus located just anterior and inferior to area VIP+ was also observed to contain a complete or partial representation of the contralateral hemifield. This area was also activated by passive finger stimulation (Huang and Sereno, 2006, submitted), and may correspond to the anterior intraparietal sulcus area (AIP) in macaque monkeys (Lewis and Van Essen 2000a, 2000b; Culham and Kanwisher, 2001; Culham, 2003; Culham et al., 2005).

**Middle Temporal areas (MT+)**

Fig. 1.6 shows retinotopic maps around area MT+, including MT, MST, FST, and V4t, on both hemispheres from five single subjects and 24-subject-average data. Yellow dashed contours indicate area MT on both polar angle and eccentricity maps. The small ellipsoidal region was drawn based on the well-defined area MT in macaque and owl monkeys (Van Essen et al., 1981; Maunsell and Van Essen, 1983, 1987; Weller et al., 1984; Ungerleider and Desimone, 1986; Kaas and Morel, 1993), and on the basis of field-sign maps calculated for the data (see below). In general, the upper field (red) is located anterior and slightly inferior to the representation of lower field (green) on the polar angle maps. The representation of the center of gaze (as indicated by an asterisk) is located inferior to the peripheral representation on the
eccentricity maps. Field sign maps (not shown in Fig. 1.6) further show that area MT contains a non-mirror image representation of the contralateral hemifield. The axes of two coordinates, polar angle and eccentricity, were not always orthogonal to each other; this probably reflects a combination of underlying non-orthogonality as well as noise due to limitations on voxel size.

There are several additional retinotopic areas around area MT. The areas anterior and superior to MT may correspond to area MST (medial superior temporal sulcus) in macaque. The areas anterior and inferior to MT may correspond to area FST (fundus of superior temporal sulcus) in macaque. These areas also contain representations of the contralateral peripheral visual hemifield, and may each have more than one part (see e.g. Kaas and Morel, 1993).

**Posterior parietal areas (LIP+)**

Figs. 1.7 and 1.8 show a close-up view of the posterior parietal cortex in several subjects. A cluster of retinotopic maps exists beyond area V3A and V7, including several areas in LIP+ along the intraparietal sulcus, which extend anteriorly into the postcentral sulcus (VIP+ and AIP). Area V7, originally defined in Tootell et al. (1998) as an area containing only upper fields, is located immediately anterior to area V3A. The lower visual field representation (green) of area V7 is located anterior and medial to the upper field representation (red) as shown in both single-subject and 24-subject-average data. The number of areas and their distribution in the LIP+ cluster is somewhat variable across subjects. At least three complete maps (tentatively labeled as LIP1, LIP2, and LIP3) of the contralateral
hemifield were consistently observed across subjects. In addition to areas LIP1-3, some small maps were located lateral to V7 and LIP1, and anterior to LIP2 and LIP3. Area LIP1, located immediately anterior to area V7, was originally defined as putative human LIP in Sereno et al. (2001). The upper visual field representation (red) of area LIP1 is located anterior and lateral to the lower field representation (green), which joins the lower field representation of V7. Area LIP2 is located anterior and medial to area LIP1, and its lower field representation (green) extends medially into precuneus. Area LIP3 is located anterior and lateral to area LIP1, and its lower field representation (green) extends anteriorly and laterally along the intraparietal sulcus. Areas LIP1-3 usually share a continuous region (red) of upper field representation, as shown in most single-subject and in the 24-subject-average maps. In some subjects, however, this upper field representation is discontinuous (for instance, see subjects 5, 8, 12, 13, and 14 in Fig. 1.8). Areas LIP1 and LIP2 may correspond to areas IPS1 and IPS2 activated by saccade eye movements (Sereno et al., 2001; Schluppeck et al., 2005, 2006). In our retinotopic mapping paradigms, the subject maintained central fixation while attending to the video contained in a rotating wedge during the entire scan. Silver et al. (2005) suggested that these areas could be driven by attention without the presence of systematic visual stimuli.

Medial parietal areas

Fig. 1.9 shows two retinotopic areas, precuneus (PreC) and V6, in polar angle maps from five subjects and the 24-subject-average map. Area PreC contains a complete representation of the contralateral peripheral visual hemifield. In some
subjects, this region contains more than one part. In general, the upper field (red) is located inferior to the representation of low field (green), which is consistently observed across single-subject data as well as in the group average data. The lower field representations (green) of area PreC and LIP2 may join each other.

Area V6, which contains a complete representation of the contralateral peripheral visual hemifield, is located at the posterior bank of the parietal-occipital sulcus (POS) (Pitzalis, et al., 2006). Some subjects show partial retinotopic activities in a region between PreC and V6. This region may correspond to areas MIP/V6A/PRR in macaque monkeys (Connolly et al., 2003).

Ventral occipital areas

Fig. 1.10 shows retinotopic maps in the ventral occipital region on flattened cortical surfaces. Areas V1+, V2+, and V3v/VP+ contain upper field representations of the contralateral hemifield. The area anterior to V3v/VP+ was originally labeled as V4v in human, and contains only an upper field representation of the contralateral hemifield (Sereno et al., 1995; Hadjikhani et al., 1998). Anterior to V4v, Hadjikhani et al. found an area V8 that contained a complete representation of the contralateral hemifield. Evidence from Wandell et al. (2005) suggested the area directly anterior to V3v/VP+ contains a complete representation of the contralateral hemifield and defined it as human V4 (hV4). Our data supports and includes both schemes in Hadjikhani et al. and Wandell et al. The principle feature in this region is a lower field representation (green) surrounded by two or three upper field representations (red). This morphology is similar to the organization of LIP+ in the intraparietal
region where a central upper field representation is surrounded by three or four lower field representations. The area labeled as hV4 in Fig. 1.10 contains a complete representation of the contralateral hemifield and its upper field portion resembles the original V4v. The horizontal meridian (blue) of hV4 is parallel to the V2/VP and VP/V4v borders.

The area anterior to area hV4 is labeled as V8, which also contains a complete representation of the contralateral hemifield. However, its horizontal meridian is perpendicular to the V2/VP and VP/V4v borders. In area V8, the center of gaze (indicated by an asterisk in the eccentricity maps in Fig. 1.10) is located anterior to its peripheral representations. The retinotopic organization and location of V8 is consistent with area VO-1 defined in Brewer et al. (2005).

An area located anterior to area V8/VO-1 also contains a complete representation of the contralateral hemifield, whose upper field joins the upper field representation of V8/VO-1. This retinotopic organization and location of this area is also consistent with area VO-2 defined in Brewer et al. (2005), whose lower field is located anterior to the upper field. In addition, our wide-field video stimuli further reveal two unlabeled areas beyond the ventral/anterior limits of V2+ and VP+. Perhaps these areas could be considered as V6 equivalents in the ventral occipital surface because of their locations and preference to the periphery.

**Discussion**

Precise retinotopic and anatomical definition of visual areas in non-human
primates has aided studies of areal function. Definition of boundaries in individual subjects is important because adjoining areas often have different response properties and because the size of a visual area is often comparable to the variability in its 3D location between brains.

In the last decade, fMRI experiments using flickering checkerboard stimuli have successfully revealed retinotopic maps in the early visual areas in humans (Sereno et al., 1995; Tootell et al., 1998, Wandell, 1999; Dougherty et al., 2003; Slotnick and Yantis, 2003; Warnking et al., 2002; Wandell et al., 2005). The luminance of black-white checkerboard stimuli has maximum contrast and is very effective for eliciting BOLD signal difference in the early visual areas (Sereno et al., 1995). This was critical during the early development of fMRI when only lower-field (e.g. 1.5 T) scanners were available. Higher-level visual areas, however, are less selective for simple visual patterns such as luminance contrasts and edges in the checkerboards. Furthermore, the checkerboard stimuli may not attract the subjects’ attention when they are required to fixate centrally. Videos, however, contain complex stimuli, such as faces, body parts, objects, and optical flow fields (generated during camera tracking movements), which are more similar to the natural scenes one observes in daily life. In this study, the video “ON vs. OFF” paradigm revealed visually-driven areas in the occipital, temporal, parietal, and frontal lobes. Phase-encoded paradigms further revealed that virtually all of the areas activated by the video “ON vs. OFF” paradigm showed some degree of retinotopy.
Parietal cortex

Beyond area V3A, a continuous strip of retinotopic areas was found along the intraparietal sulcus, extending anteriorly into the postcentral sulcus and medially into the precuneus. In area V7, the lower field is located anterior to its upper field, which joins the upper field representation of V3A. The LIP+ cluster is tentatively divided into three areas, which are posterior (LIP1), anterior/medial (LIP2), and anterior/lateral (LIP3) to a central region of upper field representation. The posterior area LIP1, defined as “putative LIP” in Sereno et al. (2001), contains a lower field representation that joins the lower field representation of area V7. Area LIP2, anterior/medial to LIP1, contains a lower field representation that extends onto the medial wall of parietal lobe, which may continue to join the lower field representation of the precuneus area (PreC). Area LIP3, anterior/lateral to LIP1, contains a lower field representation that extends anteriorly and laterally along the intraparietal sulcus, and may continue to join the lower field representation of VIP+. In area VIP+, the upper visual field representation is located medial and anterior to its lower field representation. The small maps between LIP+ and VIP+ are somewhat variable across subjects. High-resolution imaging using multi-element surface coils may be able to resolve these maps in greater detail in the future.

The existence of multiple retinotopic maps between the most posterior LIP and the most anterior VIP also suggests that the posterior parietal cortex in humans contains a more complex topology than is suggested by data from macaque monkeys (Lewis and Van Essen 2000a, 2000b; Culham and Kanwisher, 2001), although more recent anatomical findings suggest that in macaques, LIP may have five subdivisions
(Gattass et al., 2005). Single-cell recording experiments in areas LIP and VIP in the macaque monkey had suggested that these areas were not organized into retinotopic maps (Maunsell and Van Essen, 1983; Ungerleider and Desimone, 1986; Colby et al., 1988; Lewis and Van Essen 2000a, 2000b). However, these areas are much smaller than the early visual areas and contain neurons with larger receptive fields. It is difficult to perform retinotopic mapping with evenly sampled microelectrodes in awake behaving monkeys (Sereno et al., 1994). By contrast, fMRI sampling is uniform but coarser, which runs the risk of missing or blurring maps whose dimensions are close to voxel sizes (Sereno and Huang, 2006).

A new retinotopic area in humans has been reported on the medial wall, in the posterior part of the parieto-occipital sulcus (Pizalis et al., 2006). This area has an extensive representation of the periphery, and in fact is difficult to activate without a wide-field retinotopic stimulus. It might be homologous to macaque V6 (which partially overlaps with the earlier-defined PO), and possibly also to owl monkey area M, both of which were reported to emphasize the periphery. However, an alternative scheme divides PO (parieto-occipital area) into two areas, DM and POm (PO medial), and suggests that DM = V6 and POm = M (Sereno and Tootell, 2005).

**Middle temporal cortex**

A good illustration of the problems faced in drawing homologies between non-human primates and humans comes from the areas around MT/V5 (Van Essen et al., 1981; Maunsell and Van Essen, 1983, 1987; Weller et al., 1984; Desimone and Ungerleider, 1986; Ungerleider and Desimone, 1986; Boussaoud et al., 1990, 1991;
Baizer et al., 1991). In owl monkeys, MT was originally defined as a small, densely myelinated oval containing a complete representation of the visual field without any discontinuities that was direction-selective, similar to macaque V5. Later work in macaques and other monkeys showed that it was surrounded by several smaller areas, including MST (medial superior temporal area) superiorly (which itself is subdivided into two parts), FST (fundus of the superior temporal sulcus area) anteriorly and ventrally (also sub-divided into two parts), a thin crescent posteriorly (DLa/V4t/MTc) (Kaas and Morel, 1993), and possibly even a small contact with V4v/VA and/or posterior inferotemporal cortex. Some of these areas are very small; for example, the area DLa/V4t/MTc represents the entire lower quadrant in a thin strip less than 1 mm wide in owl monkeys. Retinotopically mapping such an area in humans would be difficult because the width of the entire area is probably contained within a single voxel, even after accounting for its larger than expected size in humans. In light of this, the area identified by a contrast between moving and stationary patterns (MT+) might contain areas beyond MT and MST (Smith et al., 1998, 2006).

In this study, we provide evidence that area MT contains a complete non-mirror image representation of the contralateral hemifield, with a clear center of gaze. The upper field is located anterior and slightly inferior to the representation of lower field on the polar angle maps. This finding is consistent with the results in Huk et al. (2002).
Ventral occipital cortex

In humans, evidence was presented for a color-selective area, V8, containing a complete hemifield representation anterior to upper-field-only V4v, with its horizontal meridian oriented perpendicular to the V2/VP and VP/V4v borders, its upper field medial and lower field lateral, and its center of gaze anterior (Hadjikhani et al., 1998). A second proposal is that V8 (as described above: horizontal meridian perpendicular to the V2/VP border) should be called human V4 (hV4), and that there is no additional V4v-like upper-field-only area in humans between V4 and VP (Bartels and Zeki, 2000). A third group presents evidence in favor of yet a different scheme for an upper-and-lower field human V4 (hV4): its posterior upper field portion resembles V4v, its horizontal meridian is parallel to the V2/VP and VP/V4 borders, and its center of gaze is near the confluence of the center of gaze of V2 and VP (Wade et al., 2002; Brewer et al., 2005; Wandell et al., 2005). The third group also argues for another more medially placed representation of the entire hemifield (VO-1). It should be noted that the contour plots shown in Figure 3 in Hadjikhani et al. (1998) are consistent with the existence of additional representations superior and anterior/medial to V8. In the current study, we provide evidence that supports and includes both schemes proposed by the first and the third groups.

Although retinotopic maps continue to exist beyond early visual areas, the definition of subdivisions in higher visual areas remains disputed. Field-sign maps were successfully used to identify borders in early visual areas, e.g. V1/V2 and V2/V3 borders (Sereno et al., 1995). Higher areas, such as LIP+, are considerably smaller than the early visual areas (Sereno et al., 2001). The field-sign map approach
may not work well in these areas because there is less change in the gradient of eccentricity map. Usually only one coordinate, polar angle, has been used to subdivide areas in LIP+ and in anterior ventral occipital areas (hV4, V8, and VO1-2) (Brewer et al., 2005; Wandell et al., 2005). Typically a maximum or minimum on the polar angle map corresponds to a boundary (Sereno et al., 1994), so a region of “upper field” typically overlaps two or more areas. High-resolution imaging using a multi-element surface coil may provide enough increase in signal-to-noise to allow the use of smaller voxels, which may help to resolve these issues in the future.

Conclusion

In this study, wide-field phase-encoded video stimuli retinotopically activated several well-defined visual areas, including V1, V2, V3, V3A, V4v, and MT+ as well as a number of more anterior cortical areas. These high-level retinotopic areas may serve as reference maps for studying cognitive functions, such as attention and object recognition, within the same subjects.

Retinotopy extended anteriorly along the fusiform gyrus on the ventral surface, beyond MT+ into the superior temporal sulcus and lateral sulcus, beyond LIP+ into the postcentral sulcus, and medially into the posterior cingulate cortex. Area VIP+ is located at the highest level of human association cortex in the superior part of postcentral sulcus, and contains aligned retinotopic and somatotopic maps (Huang and Sereno, 2005; Sereno and Huang, 2006). Area LIP+ contains at least three maps and is activated by delayed-saccade tasks (Sereno et al., 2001). Area MT+ includes
area MT, which contains a complete retinotopic map of the contralateral hemifield and a clear center of gaze representation (Huk et al., 2002), and its surrounding areas MST, FST, and V4t. Two retinotopic maps, area V6 and PreC, were found in the medial wall of the parietal cortex. Our data also found areas hV4, V8/VO-1, and VO-2 located anterior to area VP+(V3v) in the ventral occipital surface, which supports the scheme proposed by Brewer et al. (2005).

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The text of Chapter One, in part, is a draft for future submission for publication. The dissertation author was the primary researcher and author of this draft, and the dissertation committee chair (M. I. Sereno) was the co-author. This draft will be completely rewritten before submission for publication.
Figure 1.1. Schematic representations of video stimuli in three experimental paradigms. (A) Video ON vs. OFF contained in a circular aperture. (B) Video contained in a rotating 45-degree wedge. (C) Video contained in an expanding/contracting ring. The stimuli covered 100 degrees of visual angle as outlined by the dashed circle (not visible in actual experiments).
Figure 1.2. Retinotopic maps in early visual areas of a single subject. (Top panel) Polar angle map. Significant periodic signals (p<0.001) and their phases at the stimuli frequency (slowly rotating wedge at 8 cycles/scan) are rendered on the flattened cortical surfaces for both left and right hemispheres (LH; RH). Polar angle of contralateral hemifield is color-coded as: red [upper vertical meridian; 90°] → blue [horizontal meridian; 0°] → green [lower vertical meridian; -90°]. (Middle panel) Eccentricity map. Significant periodic signals (p<0.001) and their phases at the stimuli frequency (slowly expanding or rotating ring at 8 cycles/scan) are rendered on the same flattened cortical surfaces. Eccentricity is color-coded as: red [fovea; > 0°] → blue → green → orange [periphery; ~100°]. (Bottom panel) Field sign map. Yellow and blue areas respectively indicate mirror image and non-mirror image representations of the contralateral hemifield. The borders (white dashed lines and contours) drawn on the polar angle and eccentricity maps are derived from the boundaries between mirror and non-mirror representations in the field sign map. Visual areas V1+, V2+, VP+, V4v+, V1-, V2-, V3-, V3A, and V7 are labeled according to the borders in the field sign map (note the “+” and “-” signs used here represent upper and lower fields, respectively). Areas V8, V6, and MT (part of MT+) are outlined by white dashed contours. The asterisks indicate the estimated locations of foveal representations in several areas. Sulci (concave) and gyri (convex) are indicated by dark and light gray shading, respectively.
Figure 1.3. Visually-driven areas in the video ON vs. OFF paradigm. Significant activities (p< 0.001) during the video-ON block in a second single subject (abbreviated as Subj 2) are rendered on inflated cortical surfaces for both hemispheres. (Top row) Ventral view. (Middle row) Lateral view. (Bottom row) Medial view. Black dashed lines and contours indicated borders determined by the field sign map for the same subject. Visually-driven areas extend anteriorly along the fusiform gyrus on the ventral surface, beyond area MT/V5 into the superior temporal sulcus and lateral sulcus, anteriorly into the postcentral sulcus in the parietal cortex, and medially into posterior cingulate cortex. Several additional areas are also activated, including parieto-insular vestibular cortex (PIVC), frontal eye fields (FEF), ventral premotor (PMv), pulvinar, and lateral geniculate nucleus (LGN).
Figure 1.4. Locations of high-level retinotopic areas on inflated cortical surfaces. Both hemispheres of inflated cortical surfaces are shown in dorsal-lateral, lateral, posterior-lateral, and medial views for a single subject (Subj 2). Yellow dashed contours indicate the locations of ventral intraparietal areas (VIP+), middle temporal areas (MT+), lateral intraparietal areas (LIP+), precuneus (PreC), and area V6. These areas are further discussed for representative subjects and group average data in Figures 1.5-1.9, which contain close-up views of the cortical surface outlined by the white squares.
Figure 1.5. Polar angle maps for ventral intraparietal areas (VIP+).
The results are shown on inflated cortical surfaces at a close-up dorsal-lateral view (see Fig. 1.4) for both hemispheres of two subjects (Subj 3, 4), and two single hemispheres of two other subjects (Subj 2, 5). Results from 24-subject average are shown in the bottom rows. A yellow dashed contour, indicating the putative area VIP, is drawn on each hemisphere to facilitate reading of the maps. The putative area VIP is located at the posterior bank of the postcentral sulcus and near the confluence of the postcentral and intraparietal sulci. The upper field (red) is located anterior and medial to the lower field (green) representations. Subjects 2, 3, and 5 also show a partial or complete map in an area (tentatively labeled as AIP) anterior and lateral to area VIP. All conventions follow the top panel (polar angle map) in Fig. 1.2.
Figure 1.6. Polar angle and eccentricity maps for middle temporal areas (MT+).
The polar angle and eccentricity maps are shown on inflated cortical surfaces at a
close-up lateral view (see Fig. 1.4) for both hemispheres of five subjects (Subj 1, 6, 7, 8, 9), and for the 24-subject average. A yellow dashed contour indicates the
human middle temporal (MT) area on each hemisphere. In all subjects, the upper
field (red) is located anterior and slightly inferior to the representation of lower field
(green) on the polar angle maps. The representation of the center of gaze (as
indicated by an asterisk) is located inferior to the peripheral representation on the
eccentricity maps. The label “MT+” is used here because MT+ complex contains
MT as well as other surrounding areas, MST, FST, and V4t. STS: superior temporal sulcus. Other conventions follow Fig. 1.2.
Figure 1.7. Polar angle maps for the lateral intraparietal areas (LIP+).
The polar angle maps are shown on inflated cortical surfaces at a close-up lateral-posterior view (see Fig. 1.4) for both hemispheres of one subject (Subj 10), four single hemispheres of four other subjects (Subj 3, 9, 11, 12); both hemispheres are shown for the 24-subject average. Yellow dashed contours, indicating the putative LIP+ complex, are drawn on each hemisphere to aid reading of the maps. The topology is somewhat variable across subjects. The principle feature is a central representation of upper field (red) surrounded by at least three lower field (green) representations. Three subdivisions of LIP+ are tentatively labeled as LIP1, LIP2, and LIP3. See text for detailed discussions. STS: superior temporal sulcus; IPS: intraparietal sulcus; PreC: precuneus. Other conventions follow Fig. 1.2.
Figure 1.8. Polar angle maps of the lateral intraparietal areas (LIP+) for six additional subjects. The polar angle maps are shown on inflated cortical surfaces at a close-up lateral-posterior view (see Fig. 1.4) for left hemispheres of six subject (Subj 2, 8, 5, 12, 13, 14). All conventions follow Figs. 1.2.
Figure 1.9. Polar angle maps for the medial parietal areas.
The polar angle maps are shown on inflated cortical surfaces at a close-up medial view (see Fig. 1.4) for both hemispheres of two subjects (Subj 14, 15), six single hemispheres of six other subjects (Subj 3, 5, 6, 7, 9, 16), and 24-subject average. An area in the precuneus (PreC) contains a complete representation of the contralateral hemifield, and its upper field (red) is located inferior to the lower field representations (green). Another area V6, located at the posterior bank of the parietal-occipital sulcus, also contains a complete representation of the contralateral hemifield. In area V6, the upper field is located medial and anterior to the lower field. Areas PreC and V6 are outlined by yellow contours on each hemisphere. POS: parietal-occipital sulcus. CiS: Cingulate sulcus. Other conventions follow Fig. 1.2.
The polar angle (columns 1, 3) and eccentricity (columns 2, 4) maps are shown on flattened cortical surfaces at a close-up ventral-occipital view for both hemispheres of one subject (Subj 16), four hemisphere of four other subjects (Subj 2, 6, 7, 17) and 24-subject average. Areas hV4, V8/VO-1, VO-2 are outlined by white dashed contours. The area anterior to VP+, originally labeled as V4v, contains at least three subdivisions, hV4, V8/VO-1, and VO-2. Area human V4 (hV4) contains a complete contralateral hemifield representation, and its horizontal meridian (blue) is paralleled to the borders between V1+/V2+ and V2+/VP+. Area V8 (also labeled as VO-1) adjoins hV4 anteriorly with its lower field representations (green). The center of gaze of V8, as indicated by an asterisk, is located anterior to its peripheral representations. Area VO-2, which also contains a complete hemifield map, is anterior to V8 and they share a boundary at upper field representations (red). Other conventions follow Fig. 1.2.
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Chapter 2

Dodecapus: An MR-compatible System for Somatosensory Stimulation
Abstract

Somatotopic mapping of human body surface using fMRI is challenging. First, it is difficult to deliver tactile stimuli in the scanner. Second, multiple stimulators are often required to cover enough area of the complex-shaped body surface, such as the face. In this study, a computer-controlled pneumatic system was constructed to automatically deliver air puffs to twelve locations on the body surface through an MR-compatible manifold (*Dodecapus*) mounted on a head coil inside the scanner bore. The timing of each air-puff channel is completely programmable and this allows systematic and precise stimulation on multiple locations on the body surface during functional scans. Three two-condition block-design “Localizer” paradigms were employed to localize the cortical representations of the face, lips, and fingers, respectively. Three “Phase-encoded” paradigms were employed to map the detailed somatotopic organizations of the face, lips, and fingers following each “Localizer” paradigm. Multiple somatotopic representations of the face, lips, and fingers were localized and mapped in primary motor cortex (MI), ventral premotor cortex (PMv), polymodal zone (PZ), primary (SI) and secondary (SII) somatosensory cortex, parietal ventral area (PV) and 7b, as well as anterior and ventral intraparietal areas (AIP and VIP). The *Dodecapus* system is portable, easy to setup, generates no radiofrequency interference, and can also be used for EEG and MEG experiments. This system could be useful for non-invasive somatotopic mapping in both basic and clinical studies.
Introduction

Topographic mapping is a fundamental organizing principle of sensory systems in the brain. In primary visual cortex (V1), adjacent locations receive inputs from adjacent photoreceptors on the retina, which is known as retinotopy. Similarly, different frequencies of sounds are represented in a tonotopic map in auditory cortex. Functional magnetic resonance imaging (fMRI) has been used to non-invasively reveal topographic maps in visual, auditory, somatosensory, and parietal cortices (Overduin and Servos, 2004; Sereno et al., 1995, 2001; Sereno and Tootell, 2005; Servos et al., 1998, 1999; Talavage et al., 2004). Somatotopic mapping is more difficult than retinotopy and tonotopy, however. One major limitation for an fMRI experiment is that the physical stimulus device must be compatible with the scanner environment. Visual stimuli can be projected onto a plastic screen inside the scanner, and auditory stimuli can be delivered through MR-compatible headphones. However, in somatosensory experiments, physical touch or vibration on the body surface is required to elicit sensorimotor activations, and multiple stimulators are usually needed in order to stimulate different body parts. Active finger tapping and self-paced movements are commonly used for localizing sensorimotor sites in clinical scans. The timing, intensity, and coverage of manual stimulation generated by the subject or experimenters are not as consistent and precise as those driven by mechanical devices. However, most vibrotactile devices contain metals or electrical circuits and may not be compatible with the MR environment.

Several MR-compatible devices for somatosensory stimulation have been
proposed. Flexible shafts made of carbon fiber have been successfully used to deliver vibrotactile stimuli mechanically in the scanner (Golaszewski et al., 2002a). This device does not use any metallic component inside the scanner, and produces precise vibrating frequencies and amplitudes. Magnetomechanical vibrotactile devices (MVDs) are made of MR-compatible coils, but are sensitive to placement and orientation inside the scanner (Graham et al., 2001). A piezoceramic vibrotactile stimulator generates 1-300 Hz vibrations, but requires high voltage to produce relatively small displacements (Harrington et al., 2000; Harrington and Downs III, 2001; Francis et al., 2000; Gizewski et al., 2005; McGlone et al., 2002). Both magnetomechanical and piezoceramic vibrotactile devices lead electrical wires into the scanner, which may interfere with MR signal acquisition; furthermore, they may be heated by RF pulses if not shielded properly. Similar concerns exist for experiments that apply electrical stimulation on the skin (Blankenburg et al., 2003; McGlone et al., 2002) Pneumatically driven vibrators and air-puff devices are devoid of electromagnetic interference because they use plastic tubes and MR-compatible materials inside the scanner (Briggs et al., 2004; Golaszewski et al., 2002b; Overduin and Servos, 2004; Servos et al., 1998, 1999; Stippich et al., 1999, 2004; Zappe et al., 2004). Pneumatically driven devices usually generate tactile stimulation at lower frequency (< 150 Hz), which is sufficient for eliciting somatosensory responses. Each of the aforementioned approaches for somatosensory stimulation has advantages and limitations. The selection of devices depends on their applications in various scientific and clinical contexts.

Accurate and detailed somatotopic mapping of the human body surface will
improve basic understanding of the somatosensory system, guide neurosurgical planning, and assess plasticity and recovery after brain damage or body injuries (Borsook et al., 1998; Corbetta et al., 2002; Cramer et al., 2000, 2003; Cramer and Bastings, 2000; Cramer and Crafton, 2006; Lee et al., 1998, 1999; Moore et al., 2000b; Ramachandran, 2005; Ramachandran and Rogers-Ramachandran, 2000; Rijntjes et al., 1997). Studies using fMRI have revealed somatotopic representations of the hand, fingers, wrist, elbow, shoulder, foot, toes, lips, and tongue in human brains (Alkadhi et al. 2002; Beisteiner et al., 2001; Blankenburg et al., 2003; Dechent and Frahm, 2003; Francis et al., 2000; Gelnar et al., 1998; Golaszewski et al., 2006; Hanakawa et al., 2005; Hlustik et al., 2001; Kurth et al., 2000; Lotze et al., 2000; McGlone et al., 2002; Miyamoto et al., 2005; Moore et al., 2000a; Overduin and Servos, 2004; Ruben et al., 2001; Servos et al., 1998; Stippich et al., 1999, 2004; van Westen et al., 2004; also see reviews in Burton, 2002). The human face contains important sensory organs and is essential for verbal and nonverbal communications in daily life. However, only a few studies investigated somatotopy of the human face (including the lips and ears) using fMRI (Corbetta et al., 2002; DaSilva et al., 2002; Disbrow et al., 2000; Hodge et al., 1998; Iannetti et al., 2003; Miyamoto et al., 2005; Nihashi et al., 2002; Servos et al., 1999; Stippich et al., 1999) and other non-invasive and invasive techniques (Nguyen et al., 2004, 2005; Sato et al., 2002, 2005; Schwartz et al., 2004; Yang et al., 1993). In most studies, only two or three locations on the face were stimulated manually or automatically. Somatotopic mapping of the whole face using fMRI is challenging because of the difficulty in delivering tactile stimuli to the face surrounded by a head coil. Most of the aforementioned MR-compatible
devices have been used mainly for stimulation on the fingers. For instance, MVDs (Graham et al., 2001) may not be used for face stimulation because its coils may not be compatible with the head coil. In addition, multiple stimulators are required to cover the whole face during the same scanning session. The arrangements and fixation of multiple stimulators with respect to the face inside the head coil remain a challenging issue.

In this study, a computer-controlled MR-compatible pneumatic system was constructed and used to automatically and systematically deliver somatosensory stimuli around the whole face inside the head coil. Block-design and phase-encoded paradigms were used to map the locations and internal organization of face representation in motor, parietal, and primary and secondary somatosensory cortices. The phase-encoded technique has been successfully employed in retinotopic, tonotopic, spatiotopic, and somatotopic mapping experiments (Engel et al., 1994; Overduin and Servos, 2004; Sereno et al., 1995; Sereno et al., 2001; Servos et al., 1998, 1999; Talavage et al., 2004). In a different session, the same system and paradigms as in the face somatotopy experiment were used to map the lip and finger representations

**Materials and methods**

**Participants**

Six healthy right-handed subjects (2 males, 4 females; aged 20-30) participated in this study. All subjects participated in one fMRI session for face mapping, and four
of them participated in one additional session for lip and finger mapping. Subjects gave informed consent, according to protocols approved by the Human Research Protections Program of the University of California, San Diego.

**System design and setup**

The *Dodecapus* system is composed of the following components: a portable stimuli computer, a portable air compressor, a pneumatic control module (including control circuits and solenoid air valves), a power supply for the control module (Fig. 2.1A), a 12-channel MR-compatible manifold for face and lip stimulation (Fig. 2.1B), and a bundle of plastic tubes for finger and palm stimulation (Fig. 2.1A). All metallic and electronic parts stay in the control room, and only the manifold and plastic tubes enter the scanner room.

The manifold includes two polyvinyl chloride (PVC) blocks, twelve 25-foot plastic tubes, and twelve adjustable plastic gooseneck legs ending in nozzles. The manifold is mounted on a rail at the top of a GE (or Siemens) 8-channel head coil (Fig. 2.1B). The rail was originally designed to support a mirror for visual stimuli presentation. Each leg of the manifold is composed of 20~22 segments, a 1/16-inch round nozzle, and a fitting (Loc-Line Inc., Lake Oswego, OR) rooted to the rigid PVC base. These gooseneck segments can be assembled into any desired length with special pliers (Loc-Line). The connection between segments is tight enough to hold its position while still allowing the whole leg to be freely bent to aim it at different locations on the face and lips (Fig. 2.2) or neck and shoulders. Another set of a dozen tubes was used to deliver air puffs to the tips of 10 fingers and the palms (Fig. 2.2A).
Twenty-four air tubes were led through waveguides on the Faraday cage and twelve of them at a time were connected to a pneumatic control module in the scanner control room. These tubes can be connected or disconnected easily so that the experimenter can alternate between face-only, lips-only, face vs. lips, fingers-only, face vs. fingers, and lips vs. fingers paradigms during the same scanning session.

The pneumatic control module (Fig. 2.1A) contains twelve solenoid air valves with 5 ms response time (Numatics Inc., Highland, MI) and receives airflow from a portable air compressor in the scanner control room. The module is controlled by Transistor-Transistor Logic (TTL) pulses sent from a parallel port of a portable computer (XPC, Shuttle Inc., Taiwan) running the Linux operating system. Programs written in C/C++ with the OpenGL libraries (Silicon Graphics Inc., Mountain View, CA) enable control of visual, auditory, and somatosensory stimuli with millisecond precision from the same computer. The input air pressure (30-40 psi) was adjusted so that a 500 ms air puff could be reliably detected by the subject as a light touch. Only one valve is opened at a time in order to ensure that all air puffs have the same pressure. Each flash of a light emitted diode (LED) on the solenoid module signals an opening of an air valve, which helps with monitoring of the stimuli.

Subjects were posed in the scanner with their heads tilted slightly forward (Fig. 2.2). The tilt also created enough room for the adjustable plastic nozzles around the face (note the lower part of the face was outside the head coil). The air puffs were perceived as light, slightly cool touches to a localized region of the face. A bite bar was not used so that there was enough space around the face for the plastic nozzles and to minimize stimulation of the teeth and lips. Instead, foam padding was inserted
in the head coil to minimize head movement. To completely mask the sound of the air puffs, subjects listened (through ear plugs) to white noise delivered by MR-compatible headphones. Subjects were instructed to close their eyes and the scanner room was completely darkened during the experiment.

**Experimental paradigms**

**Block-design localizers**

Three block-design paradigms were employed to localize the cortical representations of the face, lips and fingers. Each two-condition scan consisted of eight cycles of 32-s block pairs. In the first “Face Localizer” paradigm, trains of 100-ms air puffs were delivered randomly to twelve locations on the face (Fig. 2.2A) for 16 seconds (ON-block), followed by 16 seconds of no stimulation (OFF-block). There was no delay between any two consecutive air puffs. The second “Lip Localizer” paradigm was identical to the “Face Localizer” except that all nozzles were aimed around the lips (Fig. 2.2B). In the third “Finger Localizer” paradigm, trains of 100-ms air puffs were randomly delivered to each fingertip and the palm near the base of the thumb (P1) on both hands for 16 seconds, followed by a 16-s OFF-block. One additional block-design paradigm, “Face vs. Fingers”, was employed to identify the borders between face and finger representations. In this paradigm, trains of 100-ms air puffs were delivered randomly to six locations on the right half of the face for 16 seconds, followed by 16 seconds of stimulation to the right fingertips (D1-D5) and the right palm (P1). This “A vs. B” paradigm also demonstrates the
flexible use of the Dodecapus system for stimulating different body parts during the same scan.

**Phase-encoded somatotopy**

Three phase-encoded paradigms were employed to map the detailed somatotopy within each area localized from the block-design paradigms. Each scan consisted of eight cycles of 64-s periods. In the first paradigm, trains of 100-ms air puffs were sequentially delivered to 12 evenly spaced locations on the face in a clockwise or counterclockwise direction during a 64-s period (Fig. 2.2A). The air puff stimulation always started at the upper midline of the forehead, swept down to the lower midline of the chin, then continued up the opposite side of the face. This arrangement ensured that contralateral and ipsilateral hemispheres were activated during the first and second half-cycle, respectively. 80% of the gaps between two consecutive air puffs were 100 ms, and 20% of them were 200 ms. Subjects were asked to monitor for irregularities in the air puff patterns. All subjects participated in four “Phase-encoded” face mapping scans (two in each direction) following a “Face Localizer” scan. In the second paradigm, the plastic legs were adjusted and aimed at twelve evenly spaced locations around the upper and lower lips (Fig. 2.2B). In the third paradigm, trains of 100-ms air puffs were sequentially delivered to the fingertips (D1-D5) and palms (P1) near the base of the thumbs during a 64-s period in the following order: right P1 → right D1 → right D2 → right D3 → right D4 → right D5 → left D5 → left D4 → left D3 → left D2 → left D1 → left P1. The temporal patterns of air puffs were identical in all three paradigms.
**Image acquisition**

Each experimental session consists of 5 or 6 functional scans and one structural scan. Echo-planar images (EPI) were collected during 256-s or 512-s functional scans (GE 3T Signa Excite, 8-channel head coil, single shot EPI, FOV=20 cm, 3.125x3.125 mm in-plane, 3-4 mm thick slices, 128 or 256 images per slice, 31 axial slices, 64x64 matrix, flip angle=90 deg, TE=30 msec, TR=2000 msec). Since the subject’s head was slightly tilted forward, this image prescription typically included the whole cerebral cortex without using oblique slices. Structural images (FSPGR, FOV=25 cm, 1x1 mm in-plane, 1.3 mm thick slices, 106 axial slices, 256x256 matrix) were collected at the same plane as the functional scans.

**Data analysis**

Data were analyzed using surface-based Fourier methods (Sereno et al., 1995, 2001). Functional scans were first motion-corrected using AFNI 3dvolreg (http://afni.nimh.nih.gov/afni). FreeSurfer was used to reconstruct the cortical surface for each person from a pair of hand-registered structural scans (FSPGR, 1x1x1 mm) taken in a separate session. The last structural scan of each functional session was an alignment scan (also FSPGR, 1x1x1.3 mm) acquired in the plane of the functional scans and was used to establish an initial registration of the functional data with the surface, which was then refined using manual blink comparison with the structural images to achieve an exact overlay of the functional data onto each cortical surface. To determine which areas were significantly activated as well as the phase of that
activation, a Fourier transform was computed for the time series at each voxel after removing the linear trend. An F-ratio was constructed by comparing the power of the (complex) signal at the stimulus frequency (8 or 16 cycles per scan) to the power of the noise (other frequencies). The F-ratio was then converted to a (uncorrected) p-value by considering the degrees of freedom of the signal and noise. In block-design experiments, the phase angle at the stimulus frequency was divided into two bins corresponding to activations in the ON and OFF blocks; the ON phases were displayed using a heat scale ending in white (OFF-block responses were negligible in all two-condition paradigms). In phase-encoded mapping experiments, the phase angle was displayed using a continuous color scale (red → blue → green). In both cases, the saturation of the colors was modulated by the p-value (after passing it through a sigmoid), as illustrated in the color bar insets in the Figures, effectively thresholding the data.

The software used in this process is available for free download (binaries for IRIX and Linux) at http://surfer.nmr.mgh.harvard.edu/download.html. A download that also includes retinotopy analysis tools is available at: http://kamares.ucsd.edu/~sereno/csurf/tarballs/.

**Results**

Results of functional scans were rendered on inflated cortical surfaces using FreeSurfer (Sereno et al., 1995, 2001). Figs. 2.3-2.8 show detail somatotopic maps from five subjects. Fig. 2.3 and Fig. 2.4 illustrate somatotopic representations of the
face, lips, and fingers of the same subject (JG). Fig. 2.4C shows a summary of somatotopy in this subject with outlines derived from the phase-encoded mapping scans (Figs. 2.3, 2.4A). Fig. 2.5 and Fig. 2.6 illustrate somatotopic representations of the face in four additional subjects (YT, EG, YW, MD). Fig. 2.7 illustrates somatotopic representations of the lips in two subjects (YW, MD). Fig. 2.8 illustrates somatotopic representations of the fingers in two subjects (YW, MD). The details of cortical representations of each of these body surface regions are discussed below.

**Face representations**

A 256-s “Face Localizer” scan revealed multiple areas containing contralateral and ipsilaterial representations of the face (Fig. 2.3A, 2.5, 2.6), including primary somatosensory (SI) cortex at the inferior postcentral gyrus, parietal ventral area (PV) and secondary somatosensory cortex (SII) at the upper bank of Sylvian sulcus, area 7b at the posterior end of the Sylvian sulcus, primary motor cortex (MI) and premotor ventral (PMv) on the inferior precentral gyrus (Preuss et al., 1996; Stepniewska et al., 1993), a polymodal zone (PZ) at the superior precentral gyrus (Graziano, 2001), the ventral intraparietal area (VIP) and anterior intraparietal area (AIP) at the confluence of the intraparietal sulcus and the postcentral sulcus, and a small area anterior to the middle temporal (MT) area.

An average of four 512-s phase-encoded scans (two clockwise and two counter-clockwise to cancel static delay differences) further revealed continuous somatotopic organization of the contralateral face (Figs. 2.3A, 2.5, 2.6) within each area activated in the “Face Localizer” scan. In the primary somatosensory cortex (SI),
the contralateral face is organized upright along the postcentral gyrus. The contralateral forehead representation (red) extends into the central sulcus, and cheek and chin (green) are located at the inferior postcentral gyrus. The face representation in area 7b in the posterior Sylvian sulcus is upside down. In some subjects, the lower face representation of 7b joins the lower face representation of SI (this is a so-called “congruent border”, which is often seen with visual maps: e.g., upper field visual area 1 → lower field visual area 1 → lower field visual area 2 → upper field visual area 2).

The representation of the contralateral face in secondary somatosensory cortex (SII) on the upper bank of the Sylvian sulcus is also upside down. A region at the intersection of the postcentral sulcus and intraparietal sulcus (VIP) has yet another contralateral face representation, where the upper parts of the face are represented anterior to the lower parts of the face in this region (Huang and Sereno, 2005; Sereno and Huang, 2006). Some subjects (JG in Fig. 2.3A; EG in Fig. 2.5B) also showed contralateral somatotopic organizations anterior to the central sulcus in the polymodal zone (PZ) and primary motor cortex (MI).

**Upper and lower lip representations**

A 256-s “Lip Localizer” scan revealed multiple areas of the contralateral and ipsilateral representations of upper and lower lips (Figs. 2.3B, 2.7), including primary somatosensory (SI) cortex on the inferior postcentral gyrus, parietal ventral area (PV) and secondary somatosensory cortex (SII) at the upper bank of Sylvian sulcus, area 7b in the posterior Sylvian sulcus, primary motor cortex (MI) on the inferior precentral gyrus, polymodal zone (PZ) at the superior precentral gyrus, postcentral
sulcus, and ventral intraparietal area (VIP). All lip areas except the one in SI are smaller than their adjacent face areas identified by the “Face Localizer” scan.

A 512-s phase-encoded scan further revealed the somatotopic organization (Figs. 2.3B, 2.7) within each patch activated in the “Lip Localizer” scan. In the primary somatosensory cortex (SI), the contralateral lips are organized upright along the postcentral gyrus. The contralateral upper-lip representation (red) extends into the central sulcus, and the lower-lip representation (green) is located on the inferior postcentral gyrus. The upper and lower lip representations in the secondary somatosensory cortex (SII) are small and do not have a full sweep of phases. This may reflect the lack of a full contralateral representation, or it may simply be due to the fact that the internal details of the representation are too small to be resolved by our imaging resolution (whose minimum voxel size is limited by signal-to-noise considerations). The left primary motor cortex, however, shows a complete representation of the contralateral lips. The large size of the upper and lower lip representations (Figs. 2.3B, 2.7) suggests that the lips (mouth) should be thought of as the “fovea” of the face.

**Digit representations**

A 256-s “Finger Localizer” scan revealed multiple areas of the contralateral and ipsilateral representations of fingers (Figs. 2.4A, 2.8), including primary somatosensory (SI) cortex on the superior postcentral gyrus, secondary somatosensory cortex (SII) on the upper bank of Sylvian sulcus, area 7b at the posterior end of the Sylvian sulcus, primary motor cortex (MI) at the superior
precentral gyrus, and areas in the anterior and ventral intraparietal sulcus (AIP and VIP).

A 512-s phase-encoded scan revealed some of the details of the somatotopic organization within the regions (Figs. 2.4A, 2.8) activated in the “Finger Localizer” scan. In the primary somatosensory cortex (SI), a complex pattern of activation was revealed, with clear evidence for multiple representations of each digit. Even more than in the case of the lips, the individual finger representations are right at the limit of our spatial resolution. To completely resolve the somatotopic representation of the digits, it is likely that a higher signal-to-noise surface coil is required in order to high-resolution images with smaller voxels.

Interestingly, a substantial degree of digit somatotopy was revealed just inferior to the confluence of the postcentral and intraparietal sulci in a region previously labeled PP (posterior parietal cortex), PostCS (postcentral sulcus), and/or AIP (anterior intraparietal area) (Binkofski et al., 1998; Culham, 2003; Frey et al., 2005; Lewis and Van Essen, 2000; Ruben et al., 2001). This region directly adjoins VIP, which contains mainly a representation of the face and lips (Figs. 2.3, 2.5, 2.6, 2.7). Note that the overall positioning of face and forelimb are reversed in VIP and PP/AIP (face medial, forelimb lateral) when compared to the somatomotor strip (face lateral, forelimb medial).

Face vs. Fingers

A 256-s “Face vs. Fingers” scan was designed to identify the overall borders between cortical representations of the face and fingers. Although only half of the
body surface (right face and right fingers) was stimulated, this scan revealed both contralateral and ipsilateral representations of the face and fingers (Fig. 2.4B). Contralateral to the stimulation, three main postcentral finger representations were found: SI (areas 3b, 1, 2), SII (areas PV, SII proper, and 7b), and AIP (adjacent to SI); as well as precentral finger representations: MI and PMv. Face representations were also found at three postcentral regions: SI (areas 3b, 1, 2), SII (areas PV, SII proper, and 7b), and VIP. The activated focus on the precentral gyrus was tentatively labeled PZ (as opposed to the face representation in MI or PMv). Note that the face region revealed by the “Face vs. Fingers” comparison was smaller than the face region revealed by the “Face Localizer” scan; in particular, the lateral part of AIP defined as a face representation by “Face vs. Fingers” was also activated by the “Face Localizer” comparison (face versus nothing).

The representations of the face and fingers in the left (contralateral) hemisphere generally agreed with the areas found in the “Localizer” scans. However, the right hemisphere — ipsilateral to all stimulation — also showed areas that preferred face versus fingers stimulation. The regions preferring each type of stimulation in the ipsilateral hemisphere were in similar (homotopic) positions to areas in the contralateral hemisphere.

**Discussion**

Functional magnetic resonance imaging has become a routine tool in cognitive neuroscience but is currently less used for clinical studies. Experimental setup in the
MR environment remains a challenging task, especially for somatosensory experiments. In this study, a computer-controlled, MR-compatible system was constructed and demonstrated that it can deliver air puff tactile stimuli automatically inside or near the RF head coil in the scanner bore.

Fully automatic tactile stimulation could potentially be useful for clinical situations where the patient cannot follow verbal instructions and actively generate motor responses. Self-paced stimulation — such as the venerable “finger-tapping” paradigm commonly used to localize hand somatomotor cortex — can be difficult to accurately control, even for a healthy volunteer. These problems are greatly magnified when one considers self-stimulation of the face. In our pilot experiments, the subject gently touched different part of his face with a brush while listening to verbal instructions through headphones in the head coil (Sereno and Huang, unpublished data). This experiment resulted in massive head-motion artifacts correlated with the experimental paradigm. An additional complication of self-stimulation is that brain activities elicited by active hand movements may not be distinguished from those elicited by passive tactile stimulation. These problems may be minimized if the stimuli are delivered by a well-trained experimenter (Iannetti et al., 2003; Miyamoto et al., 2006). However, this approach is practically limited to block-design paradigms (ON vs. OFF) on one or two sites during each scan. Precise manual stimulation over a large continuous body surface may be difficult. These issues make fully automatic and passive tactile stimulation a preferable solution.

The Dodecapus system can be flexibly and rapidly adapted to stimulation of the face, lips, fingers, as well as other body parts. This flexibility is important given the
extremely complex shape of the somatosensory receptor surface. The pulse sequence of air puffs of each channel is completely programmable such that one can implement experimental paradigms with various temporal and spatial patterns of air-puff patterns, e.g., stimulation on the left face vs. right face. Although the current prototype has only twelve air-puff channels, it is easily expandable by adding more pneumatic control modules and “legs” to it (Briggs et al., 2004; Zapple et al., 2004). The PC parallel port interface (8 bits) can control up to 256 channels. One limitation of pneumatically driven systems is that they generate stimulation at lower frequency than vibration-based system. Dodecapus was designed to deliver low frequency air puffs (~10 Hz) for somatotopic mapping experiments. However, one can replace the nozzle of the plastic leg with various heads or vibrators that generate high-frequency vibrations (Gelnar et al., 1998). The adjustable plastic legs of Dodecapus made it easy to precisely direct nozzles to any location on the face from various angles, which may be useful for trigeminal pain research (Borsook et al., 2004; DaSilva et al., 2002; Iannetti et al., 2003). For example, one can aim at all three trigeminal branches (V1-V3) on both sides of the face with twelve air puff legs. In addition, a plunger with a probe could be added to the end of each flexible tube. There is sufficient air pressure to drive the probe with enough force to generate a range of sensations from light touches to noxious stimulation. Finally, the air delivered through the flexible legs could be heated or cooled to measure sensitivity to temperature.

This study is a first step toward a complete non-invasive mapping of the human somatosensory cortical representation. We interpret our results first in light of previous, high-resolution microelectrode mapping of somatosensory cortex
non-human primates. Merzenich et al. (1978) initially found that the area previously identified as SI actually contained four separate representations of the body: area 3a at the fundus of the central sulcus (responding mainly to muscle receptors), and three areas responding to light touch: areas 3b and 1 containing the smallest receptive fields, and area 2 containing somewhat larger receptive fields. Other work (Coq et al., 2004; Disbrow et al., 2000; Krubitzer et al., 1995; Wu and Kaas, 2003) showed that the region originally identified as SII in the Sylvian sulcus actually consisted two separate areas, SII proper and the parietal ventral somatosensory area (PV); this pattern was common to virtually all mammals (unlike the multiple SI representations; Kaas et al., 1979; Kaas et al., 2002). Just posterior to SII proper is yet another representation, area 7b (Friedman et al., 1980), which spills out of the posterior end of the Sylvian sulcus. Finally, it was known that neurons in the ventral intraparietal sulcus (VIP) have localized receptive fields on the face (Duhamel et al., 1998); but these neurons were not thought to be arranged into a topographic map.

Our fMRI results provide evidence for somatotopic maps in all of the aforementioned areas in the somatosensory cortex, as well as areas VIP and AIP in the parietal cortex. Before comparing our results with microelectrode mapping experiments, it is important to consider the different strengths of the two methods. Microelectrode mapping has better resolution than fMRI, but it is more difficult to sample the cortex evenly with an electrode (Jain et al., 2001; Hayashi et al., 1999; Manger et al., 1996, 1997). By contrast, fMRI sampling is uniform but coarser, which runs the risk of missing or blurring maps whose dimensions are close to voxel sizes.

In SI (defined as 3a, 3b, 1, and 2), in most cases, we found evidence for
multiple representations of the contralateral face, lips, and fingers. Given the
gentleness of our stimuli, we did not expect to activate area 3a. However, in most
cases we were not able to positively distinguish the representations in 3b, 1, and 2.
An additional difficulty in distinguishing these areas is that we only mapped one
coordinate of the two-dimensional somatosensory maps (face polar angle but not
face 'eccentricity' [radial distance from the mouth]; digit numbers but not distance
from the base of the finger). This will have to wait for the construction of a
stimulation device with a higher nozzle count (Zappe et al., 2004) combined with
higher resolution scans using a surface coil. Nevertheless, the repeated
representation of particular face locations, lip locations, and finger locations in
virtually every scan strongly suggests that there are multiple representations of the
face, lips, and fingers in human SI (see also Blankenburg et al., 2003; Moore et al.,
2000a; Kurth et al., 2000; Overduin and Servos, 2004; van Westen et al., 2004).

We also found evidence for multiple representations of the body in the Sylvian
sulcus in the regions expected to be occupied by PV, SII proper, and area 7b. The
strongest evidence for three representations in this region is seen in Fig. 2.4B, left
(contralateral) hemisphere, where three face and three finger representations are
clearly visible in the Sylvian sulcus.

The face localizer scan activated several areas anterior to MT (as defined in
these subjects by retinotopic mapping; data not shown) which have been previously
reported for moving tactile stimuli on the hand (Hagen et al., 2002; Blake et al., 2004;
Beauchamp, 2005). The activated region was somewhat variable across subjects (Figs.
2.3A, 2.5, 2.6). In most cases, the activated region adjoined MT but in a few instances,
the activated region was found near the STS.

Finally, we corroborated our finding of face somatotopy in area VIP (Huang and Sereno, 2005; Sereno and Huang, 2006). Additionally, we found evidence for a small representation of the lips in area VIP. Immediately adjacent to VIP, we found strong evidence for passive finger somatotopy in an area just inferior to the confluence of postcentral and intraparietal sulci. This area has been labeled PP (posterior parietal) by Ruben et al. (2001) and “PostCS” region by Culham (2003). We suggest that this area may correspond to a human homologue of AIP (Binkofski et al., 1998; Culham et al., 2005; Frey et al., 2005; Lewis and Van Essen, 2000). These results suggest that AIP and VIP form a third tier of somatotopic maps that have multisensory properties. We might expect to find a more lateral part of AIP that represents the foot independent from those in PV, SII proper, and 7b. The evidence from Golaszewski et al. (2006) may be consistent with this idea.

Conclusions

A computer-controlled MR-compatible system was constructed to automatically and independently deliver light air puffs to twelve locations on the body surface through a manifold (Dodecapus) inside the magnet. While we focused primarily on face stimulation, this flexible system can also deliver air puffs to lips, fingers and other body parts during the same scan. Two-condition block design paradigms were employed to localize the representations of the face, lips and fingers in the primary and secondary somatosensory, parietal, and motor cortices.
Phase-encoded paradigms were then used to reveal the internal organization of the somatotopic maps in these areas. This system is easy and quick to setup, and may be useful for non-invasive somatotopic mapping in both basic and clinical studies.

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Figure 2.1. Apparatus. (A) System layout. (B) Dodecapus manifold. The manifold is mounted on top of the head coil by sliding its base into the head coil mirror rail. The “legs” are connected to the solenoid valves by long plastic tubes that run through waveguides.
Figure 2.2 Demonstration of experimental setups. (A) Face and fingertip/palm stimulation. During the actual experiment, the subjects rested their hands on their abdomen, and wore earplugs and headphones. Note that an exit hole was drilled on the external corner of each PVC pipe elbow to provide an outlet for the airflow, which ensured that only the fingertips were stimulated. (B) Air puff nozzles around the lips. Subjects closed their mouth and eyes during the actual experiment.
Figure 2.3. Face and lip somatotopy of a single subject (JG). (A) Face maps. (B) Lip maps. Somatotopic maps of face or lips were rendered on inflated cortical surfaces (lateral view) for “Localizer” (top) and “Phase-encoded Somatotopy” (bottom) scans, respectively. Regions activated during ON-block in “Localizer” scans were rendered with heat scales (white). Three main clusters of somatosensory areas were activated: primary areas (3b, 1, 2), secondary areas (PV, SII-proper, 7b), and parietal areas (VIP and AIP) (see text for other areas). Polar angles of contralateral face and lip somatotopy were color-coded: $90^\circ$ (red) $\rightarrow 0^\circ$ (blue) $\rightarrow -90^\circ$ (green). The insets show the significance thresholds. Sulci (concave) and gyri (convex) are indicated by dark and light gray shading, respectively. Gray solid contours indicated the outlines of the central, postcentral, intraparietal, and Sylvian sulci. Gray dashed contours indicate fundi. White dashed contour represents the boundary of area MT as determined in retinotopic mapping experiments from the same subject. STS: superior temporal sulcus; LH: left hemisphere; RH: right hemisphere.
Figure 2.4. Finger somatotopy and summary of same subject (JG). (A) Finger maps. (B) Face vs. finger representations. (C) Summary of somatotopy. Somatotopic maps of fingers were rendered on inflated cortical surfaces (lateral view) for “Localizer” (top) and “Phase-encoded Somatotopy” (bottom) scans, respectively. Regions activated during ON-block in “Localizer” scans were rendered with heat scales (white). Contralateral somatotopy of fingers and palms was color-coded: P1 (red) → D1 → D2 → D3 (blue) → D4 → D5 (green). In (B), regions activated during “right face versus right fingers” stimulation were rendered in red and green, respectively. Other conventions follow Fig. 2.3.
Figure 2.5. Face somatotopy for the second and third subjects. (A) Subject YT. (B) Subject EG. A similar cluster of areas to those shown in Fig. 2.3 was activated in these two subjects. All conventions follow Fig. 2.3A.
Figure 2.6. Face somatotopy for the fourth and fifth subjects. (A) Subject YW. (B) Subject MD. Note that activations found in primary and secondary auditory cortex (AI/AII) in (B) were likely due to poor masking of air puff noise (masked well in all other experiments). Again, a similar set of area clusters were activated. All conventions follow Fig. 2.3A.
Figure 2.7. Lip somatotopy for the fourth and fifth subjects. (A) Subject YW. (B) Subject MD. Lip localizer scans revealed a lip representation within VIP. Phase-encoded mapping showed somatotopy within the primary and secondary clusters. All conventions follow Fig. 2.3B.
Figure 2.8. Finger somatotopy for the fourth and fifth subjects. (A) Subject YW. (B) Subject MD. Note the extensive passive finger somatotopy in are AIP in the left hemisphere of the fifth subjects (bottom left), which closely resembles activations seen in the first subject (Fig. 2.4A). All conventions follow Fig. 2.4A.
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Chapter 3

A Human Parietal Face Area Contains Aligned Head-centered Visual and Tactile Maps
Abstract

Visually-guided eating, biting, and kissing, and avoiding objects moving toward the face and toward which the face moves require prompt, coordinated processing of spatial visual and somatosensory information to protect the face and brain (Cooke and Graziano, 2004; Bremmer, 2005; Grefkes and Fink, 2005). Single-cell recordings in parietal cortex identified multisensory neurons with spatially-restricted, aligned visual and somatosensory receptive fields (Duhamel et al., 1998), but so far, there has been no evidence for a topographic map in this area. Here, we map the organization of a multisensory parietal face area in humans by acquiring functional magnetic resonance images while varying the polar angle of facial air puffs and close-up visual stimuli. We found aligned maps of tactile and near-face visual stimuli at the highest level of human association cortex in the superior part of the postcentral sulcus. We then show that this area may code the location of visual stimuli with respect to the face, not with respect to the retina.

Introduction

In macaque monkeys, neurons in a multisensory parietal area at the border between visual and somatosensory cortex -- the ventral intraparietal area, VIP -- were discovered to have spatially-restricted visual and somatosensory receptive fields that were aligned with each other. For example, a VIP neuron with a visual receptive field in the upper right part of the visual field will also typically have a somatosensory
receptive field located on the upper right part of the forehead. VIP neurons respond selectively to optical flow stimuli (Colby et al., 1993; Duhamel et al., 1998; Bremmer et al., 2002), and have connections with visual motion areas, somatosensory areas, and motor areas controlling face and eye movements (Lewis and Van Essen, 2000). Electrical stimulation of VIP results in defensive movements including flinching (Cooke et al., 2003).

The mobility of the eyes with respect to the face and head, however, could potentially misalign somatosensory and visual inputs. There is evidence that some VIP neurons remap their visual receptive fields to cancel the effects of eye movements (Duhamel et al., 1998; Avillac et al., 2005), using information about eye position. Thus, if the monkey moves its eyes downward so that the visual stimulus moves further into the upper visual field with respect to the retina, the visual receptive field will nevertheless maintain its alignment with the upper right forehead rather than moving downward with the retina. These VIP neurons thus represent both visual and somatosensory information in a somatosensory coordinate system. This stands in contrast to the nearby lateral intraparietal area, LIP, which represents and updates potential visual targets -- including those initially detected by way of another modality -- in a visual (retinotopic) coordinate system (Colby et al., 1996; Grunewald et al., 1999).

Previous functional magnetic resonance imaging studies of multisensory processing in humans by Bremmer and others (Bremmer et al., 2001; Culham and Kansisher, 2001) have shown using conjunction analysis that there is a small region in parietal cortex that responds to somatosensory, visual, and auditory stimuli like
monkey VIP. In both human and monkey, however, there has been no evidence that this region contains retinotopic or somatotopic maps of near-face space. Earlier studies of LIP in humans, which is situated just posterior to the multisensory focus, showed that potential visual targets there are in fact represented in a retinotopic cortical map (Sereno et al., 2001; Medendorp et al., 2003; Merriam et al., 2003). This study set out to determine if human VIP, too, contains a topographic map -- but in this case, a multisensory map in which visual space is superimposed and aligned with a somatosensory map.

**Methods**

**Subjects**

Subjects (n=12) were male and female students, faculty, and staff of the University of California, San Diego, with normal or corrected-to-normal vision. Each participated in 1-5 fMRI imaging sessions. Informed consent was obtained according to procedures approved by the UCSD Human Research Protections Program.

**Somatosensory stimuli and tasks**

For somatosensory stimuli, an air compressor in the scanner control room provided input to a 12-way solenoid manifold valve (Numatics) that was controlled by TTL pulses from a stimulus computer parallel port. 12 plastic air tubes from the manifold valve passed through waveguides into the scanner room and then into the magnet, where they connected to a block mounted on the head coil that served as a rigid base for 12 flexible tubes with nozzles (Loc-Line) that could be freely
positioned in order to direct air puffs at 12 locations around the person’s face. The input air pressure (30-40 psi) was adjusted so that a 500 msec air puff could be reliably detected by the person. The air puffs were perceived as light, slightly cool touches to a localized region of the face. They were presented either in block designs (ON vs. OFF, left face vs. right face), or in mapping experiments (one cycle around the face, clockwise or counterclockwise, every 64 sec) while subjects monitored for occasional gaps in an otherwise equally spaced sequence.

**Visual stimuli and tasks**

For visual optical flow stimuli, an in-house program (original by Anders Dale) contrasted 16 sec blocks of coherent motion with scrambled motion. A new field of white dots was generated every 500 msec. Dots immediately began to move along a trajectories so as to generate a coherent movement on a plane. The motion was chosen randomly for that 500 msec period from a continuum that ranged from dilations to outward spirals, to rotations, to inward spirals, to contractions. The center of the movement was jittered, and the speed varied within a small range. During the scrambled OFF period, dots and their movement vectors were generated as during the coherent ON periods except that each dot was rotated a random angle around the pattern center before its path was executed. This scrambled the movement (at a given point, dots moved in different directions), but preserved the speed gradient (central dots still moved slower than peripheral dots).

For retinotopic visual mapping stimuli, in-house OpenGL programs generated either a standard flashing checkerboard rotating wedge (original version by Anders
Dale) or video wedge stimuli (by M.I.S.) on an SGI O2. In both cases, the wedge moved smoothly. For video, a black mask containing a 45-degree-wide wedge-shaped aperture was drawn on top of each NTSC input frame (from episodes of Xena the Warrior Princess) in real time. The aperture slowly rotated around a central fixation cross (one cycle every 64 sec). Each video frame was scaled down to the approximate size of the aperture and then translated so that the center of each frame always appeared at the center of the slowly rotating aperture. Subjects fixated a central cross for the duration of the scan (stability verified by tests with a pupillometer outside the scanner) and in the case of video stimuli, attempted to follow the story.

To test for head-centered visual representations, we had subjects track a fixation point in the center of a ~20 degree circular aperture containing video (same source as above) as the aperture and superimposed fixation cross moved periodically around the person's face along a ~50 degree diameter circular path. Video frames were scaled and centered within the aperture before the mask was drawn as in the video retinotopy stimulus. Central and near peripheral retinal stimulation is approximately constant in this case but the stimulus periodically varies its position with respect to the head and face. Periodic activation by this stimulus is consistent with a head-centered visual representation. The phase of the periodic response can be used to estimate the angle to which central receptive fields have been remapped.

Data acquisition and analysis

Echo-planar images were collected during 512 sec runs (3T GE Signa Excite, 8-element phased-array head coil, single shot EPI, 3x3 mm in-plane, 3-4 mm thick
slices, 256 images per slice, 31 axial slices, flip angle = 90 deg, TE = 30 msec, TR = 2000 msec, 64x64 matrix, bandwidth = 1800 Hz/pixel). A total of 204 functional scans were performed on 12 persons including at least 6 face air-puff scans and 8 scans to map visual areas per person. Functional scans were motion-corrected using AFNI 3dvolreg. FreeSurfer was used to reconstruct the cortical surface for each person from a pair of registered structural scans (FSPGR, 1x1x1 mm) taken in a separate session. The last scan of each functional session was an alignment scan (also FSPGR, 1x1x1.3 mm) acquired in the plane of the functional scans and used to establish an initial registration of the functional data with the surface, which was then refined using manual blink comparison with the structural images to achieve an exact overlay of the functional data onto each cortical surface. To increase signal-to-noise, we typically combined four 512 sec scans for each task.

To determine which areas were significantly activated as well as the phase of that activation, a Fourier transform was computed for the time series at each voxel after removing the linear trend. An F-ratio was constructed by comparing the power of the (complex) signal at the stimulus frequency (8 or 16 cycles per scan) to the power of the noise (other frequencies). Very low frequencies (movement artifact) and harmonics were excluded. The F-ratio was then converted to a (uncorrected) p-value by considering degrees of freedom of the signal and noise. In two-condition experiments, the phase angle at the stimulus frequency was divided into two bins corresponding to responses to ON and OFF blocks, and the ON phases displayed using a heat scale ending in white (OFF block responses were negligible in all four two-condition experiments). In mapping experiments, the phase angle was displayed
using a continuous color scale (red \(\rightarrow\) blue \(\rightarrow\) green). In both cases, the saturation of the colors was modulated by the p-value, as illustrated in the color bar insets in the Figures.

**Surface-based cross-subject average map**

A 9-person, 32-scan cross-subject average map was constructed by morphing individual brain surfaces into alignment with an average target brain, sampling the data onto a subtessellated icosahedron, combining the complex signals by vector averaging after reversing phase as appropriate (the vector sum strongly penalizes inconsistent phase across scans and corrects for stationary between-voxel differences in hemodynamic delay), and then sampling the statistic back onto an individual brain, all using FreeSurfer. 3 out of 12 subjects whose data was most contaminated by movement artifact were omitted from the average.

The software used in this process is available for free download (binaries for IRIX and Linux) at http://surfer.nmr.mgh.harvard.edu/download.html. A download that also includes retinotopy analysis tools is available at http://kamares.ucsd.edu/~sereno/csrf/ tarballs/. AFNI tools can be found at http://afni.nimh.nih.gov/afni/.

To obtain 3D coordinates compatible with previous studies, we used the Montreal Neurological Institute Automated Linear Registration Package to generate Talairach transformation matrices (Colline et al., 1994) available for free download as MNI autoreg at http://www.bic.mni.mcgill.ca/software/distribution/. The average Talairach coordinates for the center of mass of VIP across the 9 subjects in the right
and left hemispheres were (30, 43, 59) and (-28, -46, 58) with standard deviations (4, 5, 6) and (4, 7, 6) (all in mm).

**Nomenclature**

The nomenclature of areas in human intraparietal sulcus is not completely settled (Sereno and Tootell, 2005). Here are some correspondences with studies not otherwise mentioned. The most anterior parietal focus in Figure 1 in Culham et al. (1998) is very close to VIP as defined here. The area labeled "DIPSA" in Figure 1 of Orban et al. (2003) is close to our VIP (the region they label "VIPS" has been labeled V7 in several other studies). The region labeled "VIP/SPO" in Figure 2 of Tootell et al. (1996) is similar to area V6 as defined in Pitzalis et al., (2004) and posterior and medial to our current VIP. The area labeled "aIPS (VIP/LIP)" in Astafiev et al. (2003) is similar to our VIP. There appears to be a multisensory cortical area in a similar relative location to VIP in both cats (rostral lateral suprasylvian sulcus, r-LS) and rodents (rostrolateral, RL). As with VIP, these areas lie at the border between unimodal visual and somatosensory areas, they are anterior and superior to most other extrastriate visual areas, and they are distinctly medial to the representation of the face in primary somatosensory cortex. In cats, area r-LS, which is just posterior to the fifth somatosensory area (SV, not equivalent to area 5), receives input from motion-sensitive lateral suprasylvian areas just posterior to it as well as registered somatosensory inputs (Mori et al., 1991; Monteiro, 2003). In rats, area RL contains a mostly lower visual field representation superimposed on a representation of the vibrissae (Tomas and Espinoza, 1987; and unpublished mapping experiments by M.I.
Cortical connections with area VIP in monkeys (Lewis and Van Essen, 2000) include: (i) areas sensitive to visual motion (PO/V6, MDP, MSTd, FST, LIP), (ii) areas that could be the source of somatosensory input from the face (strong connections from 5 and 7b, and moderate from S-II and area 2), and (iii) anterior areas associated with movements of the face and eyes (4, 6, cingulate motor area 24d). Frontal connections include the recently described polysensory area on the precentral gyrus 1 that has been shown to modulate defensive movements of the face and torso.

Results

Subjects (n = 12) were posed in the scanner with their heads tilted slightly forward so that they could directly view (without a mirror) a wide-field visual stimulus projected onto a translucent back-projection screen very close to their face. The tilt also made it possible to deliver gentle, computer-controlled air puffs to 12 approximately equally spaced locations (Fig. 3.1f) around their face through adjustable plastic nozzles (Fig. 3.1g -- the near-face back-projection screen has been removed). Subjects listened (through ear plugs) to white noise in MR-compatible headphones to completely mask the sound of the air puffs. Data were analyzed using surface-based Fourier methods (Sereno et al., 1995).

Identification of a new parietal face area

Four different block-design stimulus paradigms (Fig. 3.1a-d) were first
employed to identify areas of interest and to make a connection with previous studies. The first, “Whole Face Air Puffs vs. OFF” (Fig. 3.2b, data shown on *dorsolateral* view of inflated surface), compared 16 sec periods of randomly located facial air puffs to 16 sec periods of nothing, with eyes closed in the dark. As expected, this strongly activated face primary somatosensory cortex (areas 3b, 1) on the posterior bank of the central sulcus as well as secondary somatosensory cortex (areas S-II, PV, not visible in this view) on the upper bank of the lateral sulcus. Another area in superior parietal cortex (dotted red circles in Fig. 3.2b) was bilaterally activated as strongly (3-5% peak-to-peak signal amplitude) as primary somatosensory cortex. This area was located at the confluence of the postcentral and intraparietal sulci, near “region 1” in Bremmer et al. (2001). Its center is indicated in Figure 3.2a for the right hemisphere by the red crosses on the slice views, and on folded and unfolded cortical surface reconstructions. Very similar results were obtained when central fixation on an otherwise blank screen replaced eyes-closed (data not shown).

A second block design experiment comparing air puffs at random locations on the right half of the face versus the left half of the face (again in the dark) resulted in similarly strong activations in primary and secondary somatosensory cortex, but also in the superior parietal focus. The results are plotted in Figure 3.2c by illustrating regions that were significantly more strongly activated by stimulation of the contralateral face (no region was more strongly activated by the ipsilateral face). This result was expected in primary and secondary somatosensory areas since these areas are known to have receptive fields mainly on the contralateral half of the skin surface; but it also turned out to be the case in the red-circled superior parietal region,
indicating that this area might be somatotopic as well.

The third and fourth block-design experiments showed that the red-circled superior parietal region is also strongly visually responsive (circles are in same position across all conditions to aid comparisons). A contrast between structured moving random dot fields (dilations, contractions, spirals, rotations) and scrambled moving dot controls both viewed while fixating a central cross resulted in strong activation in parts of areas V3A, V6 (Pitzalis et al., 2004), and the anterior parts of the MT complex (possibly similar to macaque area MSTd); this optical flow stimulus also activated several parietal regions, including both LIP+ (Sereno et al., 2001; Schluppeck et al., 2005) and the red-circled region previously activated by the air puffs (Fig. 3.2d). The circled region was also strongly activated by a viewing a naturalistic moving visual scene (portions of episodes of a television action show) while fixating a central cross (relative to periods of fixating the central cross against a black background). This last paradigm was used to outline the entire extent of visually-driven cortex (Hasson et al., 2004) (Fig. 3.2e).

**Aligned multisensory maps**

To determine whether the multisensory superior parietal focus contained aligned somatosensory and visual maps we did two additional experiments. First, we adapted a stimulus method initially developed for mapping retinotopic visual polar angle representations (Engel et al., 1994; Sereno et al., 1995) to the somatosensory system. Starting near the midline of the forehead, a computer-controlled train of air puffs successively visited each of 12 locations around the face (multiple short puffs at each
location, Fig. 3.1f), slowly cycling once around the face every 64 sec for 8 cycles per scan. Subjects monitored for occasional temporal irregularities in the sequence. To improve signal-to-noise, we averaged four such scans for each subject. To correct for systematic regional variations in the shape of the hemodynamic response function, we interleaved clockwise and counterclockwise progressions (2 scans each) and then combined opposite direction data by vector addition of the complex-valued signal (the strength and phase of the response at the stimulus frequency) after reversing the phase of one direction. The somatosensory maps were then compared with maps generated by retinotopic mapping experiments using video stimuli contained within rotating wedges in the same subjects (4-scan averages, 2 clockwise, 2 counterclockwise, from a different session). By projecting the visual stimuli onto the close-up direct-view screen, a much larger field of view (100 deg visual angle) was addressed than is typical for retinotopic mapping experiments. This was critical in order to map the part of the visual field that would typically be stimulated by a naturalistic visual object that got close enough to the face to touch the parts of the face that our air puffs did.

Figure 3.3 shows the results of such a combined mapping experiment on the unfolded cortical surface of one person. At the top of the Figure, the polar angle map for air puffs is shown at low and high magnification with red indicating significant responses to the upper part of the contralateral face, blue to the middle of the face, and green to the lower part of the face (see Fig. 3.1e and Fig. 3.3 insets). Note that this Fourier-based mapping method only shows areas that have differential responses to facial stimulus location; regions that respond to air puffs at every location on the
face will be 'subtracted out' as surely as regions that are completely unresponsive to air puffs. Stimuli were delivered in the dark with the eyes closed. In both hemispheres (Fig. 3.3, top), the red circled region from Figure 3.2 showed a strong somatotopic response to the air puff mapping paradigm (Fig. 3.1e,f). The map was located at the confluence of the postcentral and intraparietal sulci. The upper parts of the face are represented anterior to the lower parts of the face in this region on the unfolded cortex.

Data from a visual mapping experiment collected in a separate scanning session on the same person are shown at the bottom of Figure 3.3. The close-up video mapping stimuli activated a number of retinotopic visual areas in posterior parietal, occipital, and posterior inferotemporal lobes (last two not visible in this view), all of which had been silent during the somatosensory stimuli. It also activated several areas in superior parietal cortex, one of which overlapped the map uncovered by the air puff mapping stimuli. Interestingly, the representation of visual stimulus angle closely matched the representation of facial air puff stimulus angle. The dashed yellow lines drawn around the somatosensory maps in the left and right hemispheres (top) have been superimposed on the visual maps (bottom) to aid comparisons. Upper visual fields were again found anterior to lower visual fields, suggesting that this region contains superimposed, aligned somatosensory and visual maps with respect to polar angle.

The agreement between the maps is within the limit of resolution of our mapping method, which is constrained by functional scan voxel width (~3 mm), cross-session alignment accuracy (~1.5 mm), and visual/somatosensory stimulus alignment.
accuracy (~10 deg polar angle). The visual stimuli activated a somewhat larger portion of the retinal sensory surface than the air puffs did of the facial sensory surface -- the slowly rotating wedge for visual mapping extended from near the center of gaze to the periphery while the air puffs avoided both the center of the face as well as scalp, ears, neck, shoulders, and arms, which are known to activate some monkey VIP neurons. This may explain why the visual maps extend slightly anterior to the somatosensory maps. The additional space between LIP+ and VIP in humans when compared to monkeys is not unprecedented -- for example, in humans, strongly motion-sensitive V3A is separated from V2 by another area whereas in monkeys, direction selective V3 (or DM) touch V2 directly.

The results of somatosensory mapping by air puffs (top image in each pair) and visual mapping by close-up rotating wedges containing video stimuli (bottom image in each pair) are shown for single hemispheres of 4 additional subjects in dorsolateral view in Figure 3.4. The dashed yellow contours are in equivalent positions at top and bottom to aid comparison. The location and organization of the multisensory area identified as human VIP is similar across subjects, though the exact details of the maps vary between subjects. For example, the upper face (and upper visual field) is situated anterior to the lower face (and lower visual) field in Subj's 3, 4, and 5, but Subj 2 (upper left) has a doubled representation. However, when comparing somatosensory and visual maps within subjects, the agreement is quite remarkable; for example, the somatosensory and visual maps are doubled in precisely identical ways in Subj 2.
Average face air-puff maps

To average mapping data across subjects, we first inflated each person's cortical surface to a sphere and then morphed it into alignment with an average spherical cortical surface using FreeSurfer (Fischl et al., 1999). This automatic, iterative, non-linear method aligns major sulci while also minimizing metric (local angle and local areal) distortion across the surface. Complex-valued mapping signals were then combined across subjects on a vertex-by-vertex basis by vector averaging. The average somatosensory mapping data from 9 subjects is shown in Figure 3.5, displayed back on the unfolded left and right hemispheres of one of the subjects used to construct the average (Subj 1 illustrated in Figs. 3.2, 3.3). In both hemispheres, the upper part of the contralateral face is represented anterior to the lower part of the face (lateral view at bottom, dorsolateral view at top). There is some suggestion that putative human VIP may contain more than one representation of the face (and visual field). In this respect, VIP may be similar to LIP+, which has recently been found to have multiple subdivisions in both monkeys (Gattass et al., 2005) and humans (Schluppeck et al., 2005). Higher resolution scans will be required to settle this question definitively.

Head-centered representations

Single-unit experiments have shown that the visual receptive fields of some VIP neurons are remapped into head-centered somatosensory coordinates (note that the reverse – remapping somatosensory receptive fields into retinal coordinates -- does not occur in VIP). In the experiments described above, subjects maintained central
fixation during visual mapping so that no remapping of visual inputs was required to maintain alignment with a head-centered face map. To test whether human VIP shows evidence for head-centered visual receptive field remapping, we had subjects (n=6) track a fixation point in the center of an approximately 20 degree circular aperture (containing video) as the aperture moved periodically around the person's face (Fig. 3.6, right) along a 50 degree diameter circular path. Central retinal stimulation is approximately constant in this case but the stimulus periodically varies its position with respect to the head and face. Periodic activation by this stimulus is consistent with a head-centered visual representation. The phase of the periodic response can be used to estimate the angle to which central receptive fields have been remapped, and these “gaze-o-topic” maps can be compared to retinotopic maps (Fig. 3.6, left) and air puff maps (Fig. 3.6, middle). Inspection of these maps (from the same subject) shows that all three are consistent. This result was obtained despite the fact that remapping of visual receptive fields is not found in all VIP neurons (Avillac et al., 2005). We did our best to minimize stray light. However, since a video projector cannot generate a pure black (zero brightness), the dimly lit masked portion of the projected image may have stimulated the moving retina; however, the phase of such a response would be reversed and offset by half 180 deg, and could only have canceled the signal we observed.

**Discussion**

The multisensory representation of the angular position of both a visual stimulus
as well as a somatosensory stimulus is consistent with data collected in single neurons in macaque area VIP. This data goes beyond the non-human primate data, however, in suggesting that adjacent locations on the face along with the corresponding adjacent locations in the visual field are mapped to adjacent locations on the cortex in a manner similar to what has been found in early visual areas such as V1 and V2, but also higher level parietal areas such as LIP and several frontal areas (Hagler and Sereno, 2006) in humans. A region near or overlapping our proposed VIP has been activated in a large number of neuroimaging studies and has been given a number of different names (see Nomenclature below). The registered sensory maps demonstrated here may help to more clearly define areal borders in this complex region.

Higher visual areas are often as strongly modulated by visual attention as by actual visual stimuli. For example, the retinotopic activation seen in area LIP while remembering a target at a location can be as large as the activation seen there while actually viewing the target, but ignoring it (Colby et al., 1996). Although the visual responses of VIP neurons are modulated by attention (Cook and Maunsell, 2002), it seems unlikely that visual attention could explain the activation to facial air puffs seen here in putative human area VIP since the areas that are most strongly modulated by visual attention such as LIP+, V7, and V3A were silent during air puff stimulation, as was virtually the entire occipital lobe. One occipital area at the anterior and superior edge of the MT complex was also activated by the air puffs. It is interesting to note that in macaque monkeys, a motion-sensitive area in this position, MSTd, has been found to have strong connections with VIP (Lewis and Van Essen, 2000).
The aligned somatosensory and visual maps in the human parietal face area provide a straightforward framework for coordinating information about nearby objects in the world. A venerable example of this computational motif is the layering of different sensory modalities in the superior colliculus (Calvert et al., 2004). In that case, the goal is to combine multisensory information in a retinocentric coordinate system in order to direct the center-of-gaze to visual targets worth looking at. Perhaps VIP can be thought of in a similar way, except that multisensory signals there are combined in a head-centered coordinate system for the purpose of approaching, manipulating, and avoiding objects with the face (Cooke and Graziano, 2004; Spence and Driver, 2004; Bremmer, 2005; Grefkes and Fink, 2005). It is likely to be a neocortical area of some antiquity given the centrality of saving your face.

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Figure 3.1. Experimental paradigms and stimulus apparatus. Four two-condition block design paradigms (a-d), and a phase-encoded air-puff paradigm (e) are shown at the top. In paradigms a, b, and e, trains of gentle air puffs with occasional gaps were delivered by adjustable air tubes to 12 different locations (f) on each person’s face (g). Visual stimuli were presented on a close-up back projection screen (not shown). e and f also show the color coding scheme used for the somatosensory maps in Figures 3.3-3.6 (the numbers in e correspond to the locations in f). Black bars in e represent 100 msec air puffs (not drawn to scale) with 100 or 200 msec gaps.
Figure 3.2. Somatosensory and visual stimuli activate a multisensory area in superior parietal cortex (red crosses, circles). The location of the multisensory focus is indicated in slice view and on folded and unfolded cortical surface reconstructions of the right hemisphere in at the top of the Figure (a). Results of somatosensory (b,c) and visual (d,e) block design experiments are shown below for both hemispheres of a single person. The red dashed circles are in equivalent positions to aid comparison. The single voxel time courses in b show that air puffs activated the circled area as strongly as they did S-I. The multisensory region was located in the superior part of the postcentral sulcus and on its anterior bank. While visual stimulation activated virtually the entire occipital lobe (e), occipital activation by somatosensory stimuli was confined to a region at the anterior end of the MT complex (b), possibly corresponding to area MSTd.
Figure 3.3. Aligned somatosensory and visual maps. The results of somatosensory mapping by air puffs (top) and visual mapping by close-up rotating wedges containing video stimuli (bottom) are shown for a single person in dorsolateral view. The white rectangles (top and bottom) indicate the position of the higher magnification views shown in the center of the Figure. The dashed yellow contours are in equivalent positions at top and bottom to aid comparison. The upper parts of the contralateral face (top rows, red) is overlaid by a representation of the upper contralateral visual field (bottom rows, red). A similar alignment is visible for middle (blue) and lower (green) face and visual field.
Figure 3.4. Visual somatosensory alignment for 4 additional subjects. The results of somatosensory mapping by air puffs (top image in each pair) and visual mapping by close-up rotating wedges containing video stimuli (bottom image in each pair) are shown for single hemispheres of 4 additions persons in dorsolateral view. The dashed yellow contours are in equivalent positions for each hemisphere to aid comparison. As in Figure 3.3, there is a detailed within-subject correspondence between somatosensory and visual maps.
Figure 3.5. Average somatotopic maps. A thick dashed yellow outline highlights the new superior parietal somatosensory map of the angle of face stimulation in putative human VIP, displayed on the unfolded cortical surface of one person from the average in lateral (bottom) and dorsolateral (top) views. Upper parts of the contralateral face (red) are situated anterior to middle (blue), and lower (green) parts of the face. The boundaries of the central sulcus and the confluence of the postcentral and intraparietal sulci are outlined in gray; the sulcal fundi are dashed.
Figure 3.6. Evidence for head-centered representation in human VIP. Retinotopic maps (left, central fixation), air puff maps (middle, eyes closed), and gaze angle maps (right, retinotopic stimulus constant as subject slowly tracks moving fixation point) coincide in many details in data from two single subjects (top, bottom), suggesting that some neurons in VIP may code the location of near-face objects in head-centered coordinates. The thick dashed yellow outline has been drawn in identical positions to aid comparison between conditions.
References


Chapter 4

The Engaging and Disengaging Brain: Event-related Electroencephalographic Dynamics in a Continuous Compensatory Tracking Task
Abstract

Event-related dynamics of electroencephalographic (EEG) activity in a continuous compensatory tracking task (CTT) were analyzed by independent component analysis (ICA) and time-frequency analysis techniques. In one-hour sessions, 70-channel EEG data were recorded while participants attempted to use compensatory trackball movements to keep a drifting disc close to a bulls-eye at screen center. Disc trajectories were converted into two moving-average performance measures, root mean square disc error defined as the root mean square distance of the disc from screen center in 4-s (local) and in 20-s (global) moving windows. Maximally independent EEG processes and their equivalent dipole source locations were obtained using the EEGLAB toolbox (http://sccn.ucsd.edu/eeglab). In two subjects, independent component processes in occipital, somatomotor, and supplementary motor cortices exhibited drowsiness-related tonic and task-induced phasic power increases in several frequency bands that were consistent across sessions and subjects. Tonic elevations in power spectral baseline reflected changes in arousal from low-error (alert) to high-error (drowsy) periods. Phasic increases were observed following ‘perigees,’ moments when the disc began to drift away from the bulls-eye. These results demonstrate that sub-second event-related EEG dynamics can be dissociated from fluctuating arousal states during a continuous tracking task without impulsive event onsets.
Introduction

EEG correlates of continuous human performance and alertness have been demonstrated on the order of 10 seconds to one minute [Huang et al., 2001; Jung et al., 1997; Makeig and Inlow, 1993; Makeig and Jung, 1995, 1996; Makeig et al., 2000]. For example, Makeig and Jung [1996] reported that during drowsiness, human performance in responding to above-threshold auditory targets tends to vary irregularly over periods of 4 minutes and longer. These performance fluctuations are accompanied by distinct changes in the power spectrum of the electroencephalogram (EEG) on at least two time scales: (1) Mean power at the human sleep spindle frequency (12-14 Hz) is tonically elevated during sustained periods of very poor or absent performance, but its second-to-second amplitude fluctuations are not coupled to performance differences during preceding drowsy periods (2) During periods of intermittent performance, about 10 s before undetected targets, low theta (3-5 Hz) activity begins to increase and gamma band activity (~35 Hz) begins to decrease. These phasic spectral perturbations are accompanied by parallel changes in target detection rate (performance). Both spectral power changes and performance return to baseline about 10 s after the performance lapse, producing circa 20-s cycles of relatively alert and drowsy performance and EEG.

During extended periods of drowsiness (as evidenced by poor detection performance), these phasic fluctuations are superimposed on slower tonic changes in both performance and EEG spectrum [Makeig & Jung, 1996]. However, the stimuli in this study were discrete and target presentation rate was low, thus not allowing the
study of transient brain dynamics at or below the second scale. Furthermore, the EEG data were collected at only two scalp sites, not allowing localization of the cortical sources of the spectral activity involved.

Sensory event-related potentials (ERP) index mean electroencephalographic (EEG) activities following onsets of visual or auditory stimuli. In many ERP paradigms, participants respond to stimulus events with single, discrete button presses. ERPs are then obtained by time-domain averaging EEG epochs precisely time-locked to stimulus or to response onsets [Makeig et al., 2002; Makeig et al., 2004a, 2004b]. In real life, many tasks require more or less continuous efforts to maintain appropriate behavior, instead of occasional, discretely cued behavioral choices (e.g., selective button presses).

During the course of truly continuous performance paradigms, on the other hand (such as in driving simulations), participants may receive continuous visual and/or auditory stimulation as well as continuous performance feedback. In addition, the timing of event onsets in continuous tasks, e.g. lane drifts during driving, is often not as precisely defined as for onsets of visual or auditory stimuli in standard ERP paradigms. Without precisely known time-locking events, one cannot measure consistent ERP waveforms in the averaged data. The ERP averaging technique is also limited to tasks involving discrete stimulus events, and may require a silent baseline period preceding stimulus onsets. Further, ERP waveforms may change as cognitive state changes, e.g. during the process of falling asleep [Ogilvie, 2001]. Finally, average ERPs capture only the relatively small percentage of EEG activity that is both time-locked and phase-locked to experimental events; time-locked
changes in spectral power without phase consistency are ignored by ERP measures. All these limitations make ERP measures inappropriate or insufficient for assessing event-related brain dynamics in continuous performance tasks accompanied by fluctuating states of arousal.

In this study, we applied event-related spectral perturbation (ERSP) methods [Makeig, 1993] to study event-related brain dynamics in a continuous compensatory tracking task (CTT) during which participants attempted to use a trackball to keep a randomly drifting disc in a bulls-eye at the center of screen [Makeig and Jolley, 1995]. Independent component analysis (ICA) was applied to continuous 70-channel EEG data collected in each of three one-hour CTT sessions per subject [Bell and Sejnowski, 1995; Jung et al., 2001a; Makeig et al., 1996]. Maximally independent EEG processes and their dipole source locations were obtained using the EEGLAB toolbox [Delorme and Makeig, 2004; http://sccn.ucsd.edu/eeglab]. ERSP methods were then applied to time course of each component.

The results demonstrate that brain dynamics on the sub-second to multi-second time scale linked to changes in human performance can be assessed even in a continuous, interactive tracking task. We found three clusters of independent component processes that exhibited both significant tonic differences in several frequency bands between low-error (alert) and high-error (drowsy) performance periods. Additional transient spectral perturbations were observed following disc trajectory ‘perigees,’ moments when the moving disc under partial control of the participant began to drift away from the target. Mean activity spectra and scalp topographies of components exhibiting these effects were stable across sessions both
within and between subjects.

Methods

Subjects and task

Six right-handed adults (3 males, 3 females; mean age = 27.8, SD = 6.0) with normal or corrected to normal vision were paid to participate in this experiment. All subjects gave informed consent before participating in protocols approved by an Institutional Review Board of the University of California San Diego. Subjects arrived after lunch and sat on a cozy chair 50 cm in front of a 19-inch screen in the EEG booth in which lighting was dim. Each subject took part in three one-hour sessions of a continuous visuospatial compensatory tracking tasks (CTT) in which they attempted to use a trackball (Fellowes Inc., Itasca, IL) to keep a drifting (‘wind-blown’) disc as near as possible to a bulls-eye, continuously visible in the center of screen (Fig. 4.1), by making frequent (~2/s) movements of the trackball in the direction of intended movement, producing (‘rocket-thrust’) bursts of directionally accelerated disc movement [Makeig and Jolley, 1995].

Subjects were instructed to continue to perform the task as best as they could even if they began to feel drowsy. No intervention was made when subjects occasionally fell asleep and stopped responding; subjects resumed task performance themselves after such non-responsive periods. Three out of 18 sessions were rejected because of severe noise due to poor grounding or long periods of sleepiness (> 40 min). The coordinates of the drifting disc and trackball activities were recorded.
about 14 times per second while a synchronous pulse marker train was sent to the EEG acquisition system for subsequent analysis.

Data acquisition

EEG activities were recorded from 70 scalp electrodes. Eye movements and blinks were recorded via two EOG electrodes placed below the right eye and at the left outer canthus, respectively. All electrodes used the right mastoid as reference. EEG and EOG activities were sampled at 250 Hz with an analog pass band of 0.01-100 Hz (SA Instrumentation, San Diego, CA). Data were digitally filtered with a linear 1-45 Hz FIR pass band filter before further analysis. The following paragraphs illustrate methods of behavioral and EEG data analysis for a one-hour CTT session (SY-1).

Analysis of tracking performance

Fig. 4.1 demonstrates the accumulated disc trajectory through a one-hour session for subject SY. The recorded time series of disc coordinates, x(t) and y(t), were converted into a disc error time series, d(t), measuring the radial distance between the disc and the screen center. Tracking performance was obtained by computing the root mean square (RMS) of d(t) in a moving time window. RMS disc error in a (4-s) short moving window indexed the subject’s ‘local’ CTT performance, whereas averaging performance in a longer (20-s) window reflected longer term changes in CTT performance.

Fig. 4.2A shows a 2-D disc trajectory in a single 4-s window (green and red
Fig. 4.2B shows the disc error time series, $d(t)$, in the same window. The green and red curves represent the disc trajectory from 2-s before to 2-s after a local minimum or perigee, defined as a moment at which the disc starts to drift away from the bulls-eye. Each perigee was defined as an event, and data epochs time-locked to perigees were defined as task epochs in which subjects should have attempted to use the trackball to move the disc toward screen center.

Subjects’ motor responses following perigee events were indexed by a recorded 2-D time series, vector trackball velocity $V(t)$. The blue curve in Fig. 4.2B represents the magnitude of trackball velocity, and each peak represents a trackball movement. The first peak of trackball velocity following a perigee was defined as response onset. In total, 1814 perigees were extracted from the time series $d(t)$. RMS disc errors in 4-s (local) and 20-s (global) epochs centered at each perigee. Fig. 4.3A demonstrates local and global RMS disc errors in chronological order. The session included several marked fluctuations in global tracking performance during the hour-long session. Fig. 4.3B demonstrates the same epochs sorted by RMS disc error. Here, values near zero reflect optimal tracking performance.

Artifact rejection

Between 0 and 5 bad single channel records, arising from poor skin contacts, were removed from the data before analysis. The task required continuous effort and frequent hand and finger movements, sometimes accompanied by head or neck muscle twitch artifacts in the EEG data. In addition, a few times subjects felt drowsy and yawned during the sessions. These events caused severe artifacts across all
channels in some epochs, which were identified and rejected from the continuous EEG data using routines available in EEGLAB. Other sources of artifacts (blinks, eye movements, and head-muscle artifacts) were separated from other EEG processes using ICA as described below [Jung et al., 2000; Makeig et al., 1996].

**Independent component analysis and component selection**

Maximally independent EEG processes were obtained using the extended-infomax option of runica algorithm from the EEGLAB toolbox [Bell and Sejnowski, 1995; Lee et al., 1999; Makeig et al., 1997]. The ICA unmixing matrix was trained separately for each session and subject. Each ICA training set consisted of ~2000-3500 s of continuous 65-70 channel data. Initial learning rate was 10-4; training was stopped when learning rate fell below 10-6. Seventy independent components were trained from representative session SY-1 (3322 s, 70 channels). Some independent components (ICs) were identified as accounting for blinks, other eye movements, or muscle artifacts. Components of interest were selected based on their characteristic scalp maps, dipole source locations, spectral signatures, and within subject consistency [Onton et al., 2005]. DIPFIT routines from EEGLAB were used to fit single dipole source models to the independent component processes using a four-shell spherical head model [Oostendorp and Oostenveld, 2002].

**Epoch selection and epoch segmentation**

Each local minimum (or disk ‘perigee’) in disk error time series d(t) was identified. Then, time series of each independent component activity were separated
into 4.5-s time intervals, 1.5-s preceding and 3-s following each perigee. The average ‘inter-perigee-interval’ (IPI) in 1814 epochs of the representative session SY-1 was about 2 s. Three further criteria were employed in final epoch selection. First, involuntary finger movements or trackball noise resulted in many brief and dips in d(t). Thus, perigees that were followed by an IPI of less than 1.5 sec were rejected from further analysis. Second, epochs in which the subject did not move the trackball between 200 and 2000 ms after the perigee were rejected. Third, perigee-locked epochs contaminated by muscle artifacts (excluding blinks and eye movements) were rejected.

In session SY-1, 937 out of 1814 perigees met all three criteria, and 4.5-s epochs time-locked to these perigees were extracted. Each of the selected perigee-locked epochs was associated with two values estimating local and global RMS disc errors, respectively. Error rate values were then sorted, and perigees at which both local and global error rates were in the lower 40% of the retained epochs were classified as ‘Alert’ epochs (Fig. 4.3C, blue dots). Perigees at which both local and global error rates were in the upper 40% of the retained epochs were classified as ‘Drowsy’ epochs (Fig. 4.3C, red dots). In this session, 225 (24%) and 235 (25%) perigees were classified as Alert and Drowsy, respectively.

**Time frequency analysis and event-related spectral perturbations (ERSPs)**

Time series of each component activity in each epoch were transformed into a (200 latencies by 102 frequencies) time-frequency data matrix using a moving-window average of fast Fourier transforms (FFTs). FFTs were computed
centered at 200 time points from 1 s before to 2.5 s after the time-locking perigee using a data-window length of 256 points, zero-padded to 512 points. Log power spectra were estimated at 102 linear-spaced frequencies from 0.5 Hz to 49.8 Hz, and then were normalized by subtracting the log mean power spectrum in the baseline (pre-perigee) periods. For each independent component, two event-related spectral perturbation (ERSP) images were thus obtained by averaging all time-frequency images from Alert and Drowsy epochs, respectively.

ERSP images were constructed to show potentially significant spectral perturbations (log power differences) from the mean pre-perigee power spectral baseline (p < 0.01, not corrected for multiple comparisons). Significance of deviations from power spectral baseline was assessed using a surrogate data permutation method [Delorme and Makeig, 2004]. The mean power spectral baselines for Alert and Drowsy epochs were plotted as thin black and magenta curves (Fig. 4.4, middle panels), respectively. In the resulting ERSP plots, non-significant time/frequency points were colored green.

**Tonic and phasic spectral perturbations**

The surrogate data method [Delorme and Makeig, 2004] was then employed to test the significance of tonic changes in power spectral baselines between Alert and Drowsy epochs at each frequency. Black horizontal bars (Fig. 4.4, middle panels) represent frequency ranges exhibiting significant (p< 0.01) tonic changes in mean power spectral baselines between the two groups of epochs. The non-green activities in ERSP images reflect significant transient phasic changes after the perigee. For
both Alert and Drowsy epochs, phasic power spectral envelopes (thick blue and red curves in Fig. 4.4, middle panels) were evaluated at each frequency by selecting the maximum value of the ERSP image 0-2.5 s after the perigee. Shaded areas and gaps represent significant and non-significant maximum values, respectively.

Results

Behavioral performance

All subjects reported that they felt drowsy several times during hour-long sessions. Fig. 4.2A demonstrates several fluctuations between good (alert) and poor (drowsy) tracking performance in session SY-1. The average number of epochs in all sessions of six subjects was near 1800, of which 800 were selected for time-frequency analysis.

Occipital cluster

Fig. 4.4A shows the scalp maps, dipole source locations, tonic and phasic changes in baseline power spectrum, and ERSPs for a bilateral occipital independent component from session SY-1. Dual symmetric equivalent model dipoles for this component process were located in lateral occipital cortex. The mean ERSP for Alert epochs (Fig. 4.4A, left panel, lower image) showed that high alpha band power (near 12 Hz) increased following disk perigees. Note that the frequency of power increase (12 Hz) is above the baseline spectral peak frequency (10 Hz), forming a slight
upward frequency shift in the alpha peak. Phasic changes at 18-22 Hz were weaker than in the alpha band. Broadband phasic changes (Fig. 4.4A, left panel, upper image) also occurred after the disk perigee in Drowsy epochs. The mean power spectral baseline for Drowsy epochs was larger (p<0.01) below 23 Hz relative to the mean power spectral baseline in Alert epochs. Equivalent dipoles in the symmetric source model for this independent component were located in the occipital cortex (Fig. 4.4A, right panel). Similar patterns of tonic and phasic activities were observed in an independent component with a near-identical equivalent dipole model from a second session (SY-2) of the same subject (Fig. 4.5A, left panel). Similar tonic and phasic increases in alpha band power were also present in two sessions (TP-1, TP-2) for a second subject (Fig. 4.5B and C, left panels). The second subject, however, did not show a second peak near 20 Hz in baseline power spectrum.

**Somatomotor cluster**

Fig. 4.4B shows the scalp maps, dipole source model, tonic and phasic changes in power spectrum, and ERSPs for an independent component from session SY-1 whose equivalent dipole was located in left somatomotor cortex. The mean perigee-locked ERSP for Alert epochs (Fig. 4.4B, left panel, lower image) showed increased phasic activities in the (18-25 Hz) beta band power around the disk perigee, followed by a transient increase in low alpha (8-10 Hz) activity. ERSPs of epochs in Drowsy epochs (Fig. 4.4B, left panel, upper image) showed sustained increases in EEG activity between 5 and 30 Hz after the perigee moment, strongest at high alpha (near 12 Hz) and beta (near 20 Hz). The mean alpha and beta increases persisted even
after the moment of median local maximum (apogee). The mean power spectral baseline of epochs in Drowsy epochs showed increased tonic activity between 7 and 26 Hz, though the difference was significant (p<0.01) only at alpha band. The equivalent dipole for this component was located in left somatomotor cortex (Fig. 4.4B, right panel).

Similar patterns of tonic and phasic activities were observed for a somatomotor component from a second session (SY-2) of the same subject (Fig. 4.5A, middle panel), and also in two sessions (TP-1, TP-2) of another subject (Fig. 4.5B and C, middle panels). Across the four sessions, significant tonic increases in EEG power occurred in Drowsy epochs, relative to Alert epochs, between 7 and 28 Hz, and broad phasic increases (predominantly in alpha and beta bands) also occurred. Equivalent dipole locations (Fig. 4.4B, right panel) for the somatomotor components were similar across sessions and subjects (SY-1/SY-2; TP-1/TP-2).

Central medial cluster

Fig. 4.4C shows ERSPs, scalp maps, tonic and phasic changes in power spectrum and dipole source location for a component process projecting to the central midline from session SY-1. The equivalent dipole for this component was located in the supplementary motor area (SMA) (Fig. 4.4C, right panel). The mean ERSP for Alert epochs (Fig. 4.4C, left panel, lower image) showed phasic post-perigee increases in power in the low alpha band (8-10 Hz) in Drowsy epochs, while in Alert epochs a phasic increase in power near 25 Hz appeared from the moment of median response onset to the median disc apogee (local maximum). The mean power spectral
baseline for Drowsy epochs at 8-12 Hz and 25-30 Hz was significantly (p< 0.01) stronger than in Alert epochs. Similar patterns of tonic and phasic activities were observed in a central medial component from a second session (SY-2) of the same subject (Fig. 4.5A, right panel). Results from two sessions (TP-1, TP-2) of another subject showed wide band (theta, alpha, and 13-30 Hz) phasic increases (Fig. 4.5B and C, right panels) in addition to tonic changes that were significant between 7 and 27 Hz in both sessions.

**Within- and between subject consistency**

ERSPs and spectral characteristics of independent components matching each of the three component clusters above were separated by ICA from each subject and session. Independent components were clustered based on correlations between their scalp maps and on their power spectral baselines between sessions [Jung et al., 2001b; Makeig et al., 2004a; Onton et al., 2005]. Similar patterns of tonic and phasic EEG power increases were observed both within and between subjects. Results for 15 sessions from six subjects (including sessions SY-1,2 and TP-1,2) are summarized in Table 4.1.

Fig. 4.6A shows the equivalent dipole source locations of 15 sessions for three independent component clusters found by inspection of component equivalent dipole locations and spectral profiles. Fig. 4.6B shows the mean power spectral baselines for Alert and Drowsy epochs and their mean tonic difference across 15 sessions. Despite variations in EEG recording across sessions and subjects (e.g., in scalp impedance), group mean power spectral baseline exhibited significant (p<0.05) tonic increases in
Drowsy epochs. The bilateral occipital cluster (15 components from 6 subjects, 11 fit with dual symmetric dipole models) showed increased mean tonic difference at all frequencies up to 25 Hz, which was significant below 12 Hz and also near 20 Hz (Fig. 4.6B, left panel). Component clusters showed smaller mean tonic increases (circa 1 dB) from Alert to Drowsy epochs. These tonic increases were significant between 10 Hz and 15 Hz in the somatomotor cluster (Fig. 4.6B, middle panel), and near 14 and 20 Hz in the central medial cluster (Fig. 4.6B, right panel).

**Discussion**

In most ERP paradigms, participants wait passively and respond to stimuli with discrete button presses. ERP analysis requires that EEG epochs be precisely phase-locked to stimulus or response events, and models the baseline period preceding stimulus onsets as electrically ‘silent.’ In this study, we demonstrate analysis of perturbations in EEG spectral dynamics during a continuous compensatory tracking task in which participants continuously attend the location of the drifting disc and actively try to compensate for its random wandering with roughly 2/s graded finger movements and no gaze fixation constraint. As the task comprised no abrupt stimulus onset events, it was not reasonable to perform stimulus-locked ERP analysis. During task performance, participants needed to be aware of disc approaches to and drifts away from the target at screen center, and to actively compensate for any drifts away from the target, which could begin at nearly any moment. Disc perigees, moments at which these drifts began, were identified post
hoc in the disc trajectories. Perigees were critical moments at which participant needed to switch from simply monitoring the ongoing disc movement to actively countering it’s movement using appropriate finger movements.

Here we report that statistically reliable phasic changes in the power spectra of independent component process activities occurred following disc perigees, particularly during periods of reduced and putatively drowsy performance. These phasic power increases appeared over a wide frequency range, from 1 Hz to at least 30 Hz, depending on source location and spectral characteristics of the component process, and lasted from a few hundred ms to two seconds or longer. These phasic increases were superimposed on tonic increases that occurred during periods of poor performance that we interpreted as indexing drowsiness.

Clean separation of EEG data into functionally and anatomically distinct processes has traditionally been difficult or impossible. Because of volume conduction through brain tissue, cerebrospinal fluid, skull, and scalp, activities arising from multiple brain networks all contribute to EEG data collected anywhere on the scalp. In addition, blinks, eye-movements, and muscle artifacts may also contaminate EEG data. These factors make it difficult to relate distinct EEG patterns, originating in specific brain areas, to behavior or pathology, or to identify the brain origins of distinct EEG sources. In particular, because of common volume conduction from nearly any cortical area to nearly any scalp electrode, spectral analysis of EEG data measured directly at scalp sensors is typically confounded.

Here, we used independent component analysis (ICA) to blindly separate multi-channel data sets into statistically maximally independent components arising
from distinct or overlapping brain and extra-brain networks. Time-frequency analysis could then be applied to the activations of EEG source signals as opposed to mixtures of EEG activities, minimizing potential confounds arising from volume conduction and summation of source signals at the scalp sensors. Results of this analysis show that EEG dynamics in multiple cortical source areas are altered when the brain directs engagement in the compensatory maneuvers.

Appearance of posterior alpha activity has long been noted to accompany lowered levels of attention and/or incipient drowsiness. Here, in the occipital cluster we observed three modifications of mean alpha band power. During alert performance, alpha power increased transiently following disc perigees. During periods of poor or drowsy performance, alpha power increased tonically, with still larger transient increases following disc perigees. The tonic increases during drowsy performance typically exceeded the transient increases during alert performance. Thus, during a continuous task, the mean alpha band power obtained in any short time window (e.g., 2 sec) alone cannot be considered as absolute index to alertness level. Instead, one needs to consider that transient power changes may be induced by a preceding task-relevant event. Also, near 20-sec cycles in EEG power may appear during periods of intermittent performance [Makeig & Jung, 1996; Makeig et al., 2000]. Thus, spectral power changes estimated using a longer analysis window (e.g. 20 sec or more), may provide better estimate of operant level of alertness.

EEG processes in the left somatomotor and central medial clusters also exhibited tonic increases during drowsy performance above 10 Hz (Fig. 4.6, bottom panel). These included an apparent slight upward shift, during Drowsy performance
epochs, in the base frequency of the somatomotor alpha or mu rhythm. The tonic drowsy performance-related changes in the somatomotor and supplementary motor areas were distinct from tonic power changes in the occipital cluster, which were predominantly below 12 Hz.

In the left somatomotor cluster, phasic post-perigee increases in alpha and beta band power were more prominent in Drowsy performance epochs than in Alert epochs (Fig. 4.4B; Fig. 4.5, middle panel). These phasic activities might be related to post-movement event-related synchronization (ERS) events (i.e., phasic power increases) seen to follow intentional movements [Pfurtscheller et al., 1999, 2003]. These results show, however, that phasic increases in EEG power began before subject responses and persisted during the compensatory maneuvers.

This study shows that the spectral dynamics of maximally independent EEG processes fluctuate on different time scales during continuous performance. Similar results of tonic and phasic changes of EEG dynamics have been reported for a compensatory simulated driving task [Huang et al., 2005] in which participants attempted to remain at the center of the driving lane during computer-simulated lane drifts. In those experiments, alpha power increased tonically during periods of relatively poor driving performance. In addition, a transient alpha increase, ‘rebound,’ or ‘synchronization’ was observed in independent component processes originating in posterior parietal cortex following each compensatory steering event. Thus, experimental paradigms and data analysis techniques demonstrated here might be useful for studying event-related brain dynamics in other ‘real-world’ continuous performance tasks.
We do not know the function of the increased EEG activities shown here. During drowsiness, tonic scalp EEG power is higher on average than during waking, but most reliably so only at low theta frequencies [Makeig and Inlow, 1993]. Makeig and Jung (1996) also showed large alpha and beta band post-event increases during periods of drowsy performance (1996). Phasic increases in EEG power during increased attention to the task might be expected at alpha, beta and gamma frequencies [Engel et al., 2001; Klimesch, 1999; Ward, 2003; Worden et al., 2000], given their frequent association with focused attention. Here, as in the earlier experiments of Makeig and Jung, participants may have increased the level of their ‘cognitive effort’ or ‘attention to the task’ in response to the increased level of performance challenge posed by continuing task demands during drowsiness. It might be of interest to apply further spectral decomposition methods to our data to determine if the broad mean spectral differences may mask a multidimensional palette of more specific spectral modulations, as recently demonstrated for frontal midline components in a working memory task [Onton et al., 2005].

Conclusion

This study demonstrates both tonic and phasic event-related EEG dynamics accompanying varying human performance in a continuous visual-motor task. Perigee moments, when the disc began to escape from the center of the screen, were identified post hoc as events embedded in the continuous compensatory tracking task. These events were not precisely predicatable, and continuous efforts by the participants were
required to respond to them so as to keep the disc near the bulls-eye target at screen center. Maximally independent EEG processes were obtained from the data using infomax ICA. Before perigees, at least three clusters of components whose equivalent dipoles were located in occipital, somatomotor and supplementary motor cortices, respectively, exhibited larger tonic power during low mean-performance (drowsy) periods. These component clusters also exhibited phasic power increases during brief post-perigee periods when the disc started to drift away from screen center. These phasic escape-related power increases were also larger during low-performance (drowsy) periods than during periods of good performance. Here, the threatening events (disc escapes) prompting the phasic EEG increases were not announced by any salient stimulus event, and could appear during disc movements in all screen directions. The phasic activity increases again suggest an intimate relation between EEG activity and top-down recognition of threatening events within the operant task context. We tentatively interpret the observed EEG signal increases as indexing increases in the level of tonic and phasic task engagement required to maintain performance during drowsiness.

Acknowledgments

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Table 4.1. Summary of spectral characteristics of independent component clusters

<table>
<thead>
<tr>
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<th>Occipital cluster</th>
<th>Somatomotor cluster</th>
<th>Central medial cluster</th>
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<tbody>
<tr>
<td>Baseline power</td>
<td>alpha</td>
<td>alpha, 13-30 Hz</td>
<td>20-30 Hz</td>
</tr>
<tr>
<td>spectrum</td>
<td>(15/15 sessions)</td>
<td>(15/15 sessions)</td>
<td>(15/15 sessions)</td>
</tr>
<tr>
<td>Tonic changes</td>
<td>&lt; 25 Hz</td>
<td>alpha, 13-30 Hz</td>
<td>8-30 Hz</td>
</tr>
<tr>
<td></td>
<td>(15/15 sessions)</td>
<td>(12/15 sessions)</td>
<td>(11/15 sessions)</td>
</tr>
<tr>
<td>Phasic changes</td>
<td>wide band</td>
<td>alpha, 13-25 Hz</td>
<td>theta, alpha, 13-30 Hz</td>
</tr>
<tr>
<td></td>
<td>(14/15 sessions)</td>
<td>(12/15 sessions)</td>
<td>Hz (10/15 sessions)</td>
</tr>
</tbody>
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Note: Each numerator represents sessions exhibiting similar spectral characteristics out of 15 sessions.
Figure 4.1. Accumulated disc trajectory during a one-hour session (SY-1). The white ring represents the bulls-eye displayed continuously at screen center. The solid white disc represents the drifting disc whose movements were partially controlled by the subject through trackball movements. The white double lines highlight an 8-s segment of the disc trajectory.
Figure 4.2. Disc trajectory in a single epoch. (A) Two concentric black rings represent the bulls-eyes pattern at screen center. The green and red traces show the 2-s disc trajectory before and after the local error minimum (perigee), denoted by a black asterisk. The radii of the red and blue dashed rings show RMS disc error in 4-s and 20-s epochs centered on the perigee. The black arrow represents the direction and magnitude of trackball velocity at one moment during disc approach. (B) Corresponding (red, green) time series of disc error, d(t), and (blue trace) magnitude of trackball velocity during the 4-s epoch. Each black cross identifies a trackball movement. The black cross enclosed in a red circle (‘rt’) identifies the first trackball movement (response time) after the perigee (‘pe’). The red and blue dashed lines represent RMS disc error in 4-s and 20-s epochs, respectively, centered on the perigee. Moment ‘ap’ marks the ensuing apogee.
Figure 4.3. Tracking performance. (A) Local (4-s, green curve) and global (20-s, blue curve) RMS disc error in 1814 unsorted perigee-locked epochs from a one-hour session. (B) Trials sorted according to local and global RMS disc error. (C) Scatter plots of 937 perigees. Each dot represents normalized local and global error rank for one perigee. Blue dots: ‘Alert’ epochs, defined as having local and global errors in the lower 40% of the session. Red dots: ‘Drowsy’ epochs, defined as having local and global errors in the upper 40%. Black dots: unselected perigees.
Figure 4.4. Results from a single session SY-1. (A) Occipital component. (B) Somatomotor component. (C) Central medial component. (Left panels) Event-related spectral perturbation (ERSP) images. Upper and lower images represent mean ERSPs for Drowsy and Alert epochs. Black solid lines: disc perigees (local minima in disc error). Red dashed lines: median time of corrective response onset (motor reaction time). Blue dashed lines: median time of the ensuing local maximum (apogee) in disc error. (Middle panels) Scalp maps and equivalent dipoles, plus tonic and phasic changes in mean power spectra. Thin black and magenta curves represent the mean baseline power spectrum preceding disc perigees in Alert and Drowsy epochs, respectively. Thick blue and red curves represent the maximum ERSP power in the 2.5 s following perigees in Alert and Drowsy epochs, respectively. Colored areas show frequency ranges with significant (p < 0.01) phasic post-perigee increases (yellow, Drowsy epochs; blue, Alert epochs). Black horizontal segments show frequencies with significantly larger (p < 0.01) tonic spectral power in Drowsy versus Alert epochs. (Right panels) Equivalent dipole source locations and their projections onto averaged brain magnetic resonance images. Green and magenta pins represent dipole locations and moments for corresponding components from session SY-1 and SY-2 (see Fig. 4.5A). The locations of the 70 scalp electrodes are shown in the middle panel of (C).
Figure 4.5. Within- and between-subject independent component scalp maps and power spectral changes in Drowsy versus Alert epochs. (Left panels) occipital cluster; (Middle panels) somatomotor cluster; (Right panels) central medial cluster. (A) Session: SY-2. (B) Session: TP-1. (C) Session: TP-2. See the description of the middle panels in Fig. 4.4.
Figure 4.6. Group data. (A) Equivalent dipole source locations for three independent component clusters from components of 15 sessions. (Upper images) dipole source locations; (Lower images) dipole projections on an averaged sagittal image. (B) Grand mean baseline power spectral across 15 sessions for three independent component clusters. Left axis: grand means of Alert (blue traces) and Drowsy (red traces) epoch power spectra. Right axis: grand mean power spectral increases (green and black traces) in Drowsy epoch baselines relative to Alert epoch baselines, averaged across 15 sessions. Significant across-session differences (p < 0.05) are shown in black. (Left panel) occipital component cluster; (Middle panel) somatomotor component cluster; (Right panel) central medial component cluster.
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Appendix A

High-resolution Mapping and Multisensory Interactions in the Human Parietal Face Area
High-resolution mapping and multisensory interactions
in the human parietal face area

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Introduction:

Facial sensation and motor control is intimately tied to the visual system. Activities such as visually-guided eating, biting, and kissing, as well as the avoidance of objects -- both those moving toward the face as well as objects toward which the face is moving during visually-directed navigation -- all require prompt, coordinated processing of spatial information from the visual and the somatosensory system. Neurons with spatially-restricted, aligned visual and somatosensory receptive fields have been found in the ventral intraparietal area, VIP, of macaques. Some VIP neurons represent visual information in a head-centered coordinate system. In previous experiments (Huang and Sereno, 2005, HBM), we uncovered a similar area in human parietal cortex by acquiring functional magnetic resonance images while varying the polar angle of facial air puffs and close-up visual stimuli. This area contains aligned, superimposed maps of light touches to the face and near-face moving visual stimuli.

Methods and Results:

A two-element parietal surface coil was constructed to improve SNR near the
superior parietal lobe so smaller voxels (e.g., 1.5 x 1.5 x 2.5 mm) could be used. Phase-encoded stimuli included air-puffs, video-in-a-wedge, and looming objects approached different face locations. To determine whether the human parietal face area encoded visual stimuli in head-centered coordinates, a near-face visual stimulus (television action show) in a circular aperture was periodically rotated around the face. Subjects either tracked a fixation point at the center of the aperture (to keep retinotopic stimulation constant) or made saccades to pre-calculated random points (to scramble retinotopic signals). Any persisting periodic activation matching the phase of an face air puff map or a near-face retinotopic map is consistent with a head-centered visual representation, implying that constant (or random) retinal stimulation is being dynamically mapped to head-centered locations. Finally, we had subjects imagine their face being touched, imagine eating, or imagine navigating between locations in familiar buildings (block design, fixation OFF, brief verbal cues). The internal organization and aligned somatosensory-visual map overlays in human VIP were confirmed. Results of head-centered tests in human VIP were positive in several subjects. Imagined touching, eating, and navigation moderately activated VIP or an area slightly lateral to it (other areas were more strongly activated – e.g., imagined navigation strongly activated the parahippocampal place area).

**Conclusion:**

Sensory maps persist up to the highest levels of some parts of human association cortex. Aligned somatosensory and visual maps are a straightforward way to coordinate information about nearby objects in the world that is reminiscent of the
layering of different sensory modalities in the superior colliculus. In that case, however, the goal is to combine multisensory information in a retinocentric coordinate system in order to direct the center-of-gaze to visual targets worth looking at. The human parietal face area might be thought of in a similar way, except that multisensory signals there are combined in a head-centered coordinate system for the purpose of approaching, manipulating, and avoiding objects with the face.

Figure A.1. Parietal surface coil and air-puff device.
Appendix B

Imaging Event-related Brain Dynamics during Continuous Driving
Event-related brain dynamics during continuous driving were studied using electroencephalographic (EEG) recording and functional magnetic resonance imaging (fMRI). A virtual-reality scene was constructed to simulate driving on a highway at a constant speed. Each of five right-handed subjects participated in two 1-hour sessions during which 256-channel EEG signals and driving task parameters were recorded at 256 Hz. During 1-hour continuous driving, every 3 to 7 seconds, the car was linearly pulled towards the curb or into the opposite lane, with equal probability. Subjects were required to compensate for the drift by holding down an arrow key, and to release the key when the car was steered back into the center of the left lane. The extent of each drift event was measured by the absolute maximum deviation from the cruising position at deviation onset. EEG data were analyzed using independent component analysis and time-frequency analysis using the EEGLAB toolbox (sccn.ucsd.edu/eeglab). A component with equivalent dipole sources located bilaterally in the intraparietal sulcus exhibited larger tonic alpha band power in large-error (drowsy) compared to low-error (alert) events. Alpha
power was suppressed briefly after deviation onset, then increased strongly (~10 dB) just before the subject released the key. This transient (1.5~3 s) alpha rebound activity was consistently observed during all single events, regardless of alertness levels. Other components localized to premotor, somatomotor, posterior parietal and cingulate cortices also exhibited event-related brain dynamics in various frequency bands that were time-locked to different phases of the drift events.

Subjects also participated in an fMRI driving session on a different day. The driving scene was projected onto a screen inside the scanner. Subjects steered the car using a two-key MR-compatible response box. Each subject participated in two 512-s periodic and two 1024-s random-ISI event-related scans. In the first two scans, the car drifted from lane center once every 16 sec. In the last two scans, the car drifted away every 5~10 sec. Functional data were acquired with an 8-channel phased-array head coil in a GE 3T scanner using a standard EPI sequence (TR=2 s, TE=30 ms, 64x64 voxels, 31 slices, 3.125x3.125x4 mm, 256 or 512 images). Data from the first two scans were analyzed using Fourier analysis. Significant activations plus their phases at the stimulus frequency (32 cycles/scan) were rendered onto inflated cortical surfaces using Freesurfer. Results showed that during each drift event, BOLD signals were activated, sequentially, in cingulate cortex, supplemental motor area (SMA), premotor, motor, somatosensory, and posterior parietal cortices. Data from the last two scans were analyzed using FMRLAB (sccn.ucsd.edu/fmrlab) and maps of maximally spatially independent BOLD process activities were rendered onto the inflated cortical surfaces. BOLD activities of several of these processes, active in middle temporal, posterior parietal, somatomotor,
parietal-prefrontal, dorsal lateral prefrontal, medial prefrontal and cingulate cortices respectively, were strongly correlated with driving performance. This study demonstrates how event-related brain dynamics during continuous driving may be explored using independent component analysis applied to data from multiple imaging modalities with differing spatial and temporal resolutions.
Appendix C

Mapping Cortical Representations of Body-centered Distance
Using MR-compatible Fiber Optics
Sensory surfaces are often represented as topological maps in the cortex (e.g. retinal maps, basilar membrane maps, skin surface maps). In the last decade, neuroimaging in humans has revealed many retinotopic maps of 2D visual space (polar angle and eccentricity). Much less is known, however, about the cortical representation of depth. An MR-compatible 64-channel fiber optics system was constructed to simulate the grid lights of an airport runway inside a GE 3T MRI scanner. The grid (visible during the entire session) contained 8 rows of 4 blue dots (0.25 mm) evenly distributed on a 40x16 inch foamboard. This layout provided a minimal depth cue in otherwise complete darkness. Three red dot targets were interleaved in each row of blue dots. Green fixation dots were placed centrally between rows, and only one was on at a time. The runway was placed on the subject's chest, near edge at their chin, and they viewed it directly by tilting their heads. Subjects (n=8) were scanned with an 8-channel head coil using standard EPI sequences (3x3x4 mm, 31 slices, TR=2s, 256 reps). Each subject participated in four phase-encoded fMRI paradigms. In the first paradigm, subjects fixated the most
distant fixation point while responding to targets (red dots). Starting from the first row (near), targets (each lasted for 500 ms) randomly appeared at three positions (left, middle, right) for 4s and moved on to the next row for 4s. The locations of targets wrapped around in depth (near to far) every 32s. The second paradigm was the same as the first except that the targets appeared far to near. The third and fourth paradigms were the same as the first and second except that the green fixation dot jumped randomly in depth every 21s. Data was analyzed using Fourier methods and FreeSurfer. The first two paradigms revealed topographic representations of distance in three clusters (V2/V3/V3A, V7/LIP/CIPS, V3B/V4d/KO/LO) consistent with the retinotopic stimulus and with lower field representations mapped separately using standard methods. The last two paradigms revealed topographic representations of distance only in the V3B/V4d/KO/LO cluster independent of gaze position (scrambled retinal inputs). These areas might be important for body-centered representation of 3D space.
Figure C.1. Experimental setup and MR-compatible fiber optics.