Human Primary Visual Cortex Topography Imaged via Positron Tomography

ERIC L. SCHWARTZ[1]* DAVID R. CHRISTMAN[2] and ALFRED P. WOLF[2]

[1]*Brain Research Laboratories, Department of Psychiatry, New York University Medical Center, and Rockland State Research Institute, Orangeburg, and [2]Department of Chemistry, Brookhaven National Laboratory, Upton, NY (U.S.A.)*

The visuotopic structure of primary visual cortex was studied in a group of 7 human volunteers using positron emission transaxial tomography (PETT) and ^{18}F-labeled 2-deoxy-2-fluoro-D-glucose ([^{18}F]DG). A computer animation was constructed with a spatial structure which was matched to estimates of human cortical magnification factor and to striate cortex stimulus preferences. A lateralized cortical 'checker-board' pattern of [^{18}F]DG was stimulated in primary visual cortex by having subjects view this computer animation following i.v. injection of ([^{18}F]DG). The spatial structure of the stimulus was designed to produce an easily recognizable 'signature' in a series of 9 serial PETT scans obtained from each of a group of 7 volunteers. The predicted lateralized topographic 'signature' was observed in 6 of 7 subjects. Applications of this method for further PETT studies of human visual cortex are discussed.

In recent years, significant advances have occurred in the study of visual topographic mapping in striate and circumstriate cortex of cats and monkeys[1,2]. The recent development of positron emission transaxial tomography (PETT), together with the availability of ^{18}F-labeled 2-deoxy-2-fluoro-D-glucose ([^{18}F]DG), permits an extension of studies performed with cats and monkeys to the in vivo study of human visual cortex. This technique has the potential to provide unique anatomical and functional data from the human visual system. However, in order to apply PETT to the study of human cortical functional architecture, several experimental difficulties must be addressed. The present experiment was designed to test whether human primary visual cortex could be topographically studied by the use of currently available PETT technology.

The principal experimental difficulties in applying PETT to the study of visual functional architecture in human cortex are: (1) the spatial and temporal resolution of current PETT detectors is severely limited[8] (relative, e.g. to CAT scanning or autoradiography). The PETT-III scanner used in the present work has

an inherent spatial reslution of 17 mm (full width half maximum, FWHM); (2) A difficulty common to cortical studies with PETT is caused by inter-subject variability in size and location of a given cortical area. For example, the total surface area of striate cortex (one hemisphere) in humans has been reported to vary between 1284 and 3702 mm^2 (ref. 13). This large range in surface area between individuals suggests that the location of the borders of striate cortex may also have a fairly large range between individual subjects. In animal studies, post-mortem verification of anatomical borders is standard. In PETT studies, this is not possible. In the present work, CAT scans of the subjects studied were obtained. However, the location of the borders of a specific architectonic area, in a CAT scan, is usually not possible. CAT scan data provide an anatomical reference for interpreting the PETT scan data, but provide little detailed architectonic data. Thus, some form of internal control is necessary in order to make confident statements about the relation of visual stimulation to PETT data. In the present experiment, *cortical topography* is *used to provide a land-*

---

* Address for correspondence: Brain Research Laboratories, NYU Medical Center, 550 First Avenue, New York, NY 10016, U.S.A.
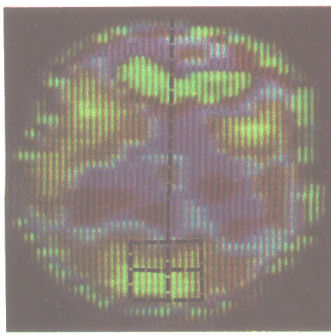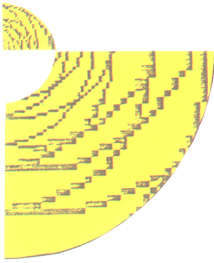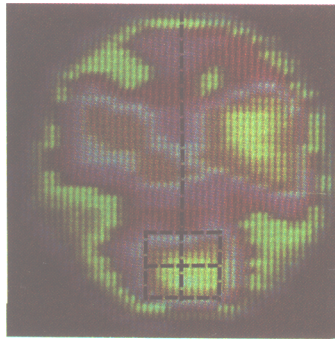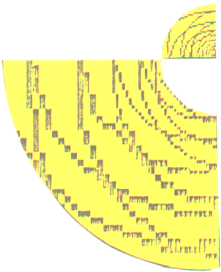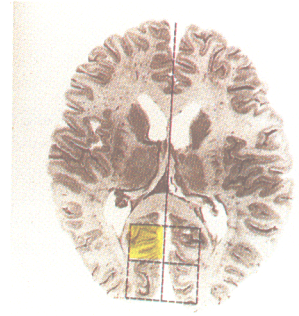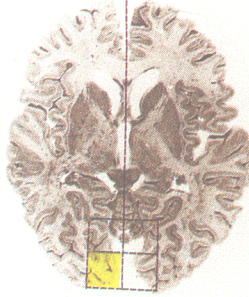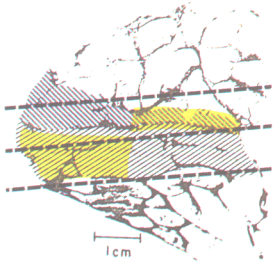
CM 4.5
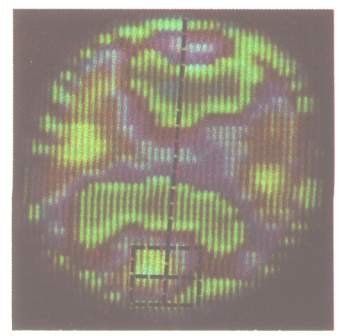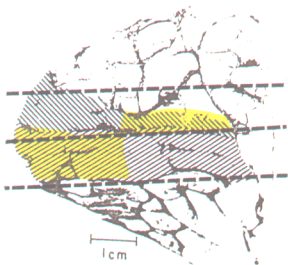
CM 5.5

SUBJECT: M.F. VS001

CM 3.9

CM 5.5

SUBJECT: G.H. VS007

mark (or 'signature')that may be used to locate prima-
ry visual cortex. This technique may then be used,
with soon to be available, higher resolution PETT
scanners (e.g. PETT-VI), for more detailed studies
of primary visual cortex topography and stimulus
preferences, as well as an aid in beginning to study
extra-striate visual areas in humans.

The present experiment was designed to study the
topographic structure of human primary visual cor-
tex, within the constraints outlined above. A quanti-
tative model of human striate cortex topography,
based on data from lower primates and human psy-
chophysical data[3,11,12] was used to guide the construc-
tion of the visual stimulus. This stimulus consisted of
a spiral pattern of 'line segments' or 'edges'. The size
of the line elements making up the stimulus was in-
creased linearly with eccentricity, in order to match
the value of cortical magnification factor at all eccen-
tricities. Estimates of human cortical magnification
factor[3] suggest that the cortical representation of a
circle at about $10°$ of eccentricity divides the striate
cortical representation into a central and peripheral
region of roughly equal areas. This circle, at $10°$ of
eccentricity, and the horizontal meridian, divide the
striate cortex representation (one hemisphere) into 4
equal areas. The computer animation used in this ex-
periment utilized a configuration of this sort (Fig. 1)
to stimulate an on–off pattern in striate cortex which
consisted of a coarse *2 x 2* 'checkerboard', in one
hemisphere. This constituted the 'signature' which
was to be located in the PETT data. A computer an-
imation was constructed by generating a stimulus
configuration as described above (and shown in
Fig. 1) onto a television monitor, and then filming
(with a computer controlled camera) frame by frame
onto 8 mm film.

Eye position of subjects was monitored and con-
trolled by requiring subjects to report verbally the
identity of small test letters ($1°$ in size) which were
randomly presented at the fixation point. These test
letters were constructed by the same computer
graphic method as the line elements of the stimulus,
and were part of the same computer animation. The
interval between presentation of the test letters was
random, with an average of 1 s. The duration of pre-
sentation was 200 ms. Since this is too short a time for
a saccadic eye movement, and since the letters were
too small to be correctly identified from non-foveal
fixations, a high score ($>80\%$) on this task implied an
accurate and reliable eye fixation. In addition, this

Fig. 1. Top: on the top left is shown a single frame from the computer animation which was used as a stimulus. Not shown is a small fix-
ation letter, which was presented at the center of the semi-circular pattern. In this example, the superior central and inferior peripheral
right hemi-fields were stimulated. The size of the pixels used in the display increased linearly from the fovea, in order to match recep-
tive field size and spatial frequency sensitivity of cortical cells at all eccentricities. The size of the pixels in the central field representa-
tion was about 1/5 degree (i.e. 5 cycles/degree). The orientation and spatial position of local stimulus elements were varied during vis-
ual stimulation. On the top center and top right are shown reconstructed PETT data obtained following visual stimulation. The mid-
line is indicated by a line, and a small region in the area of the identified primary visual cortex topographic signature is shown enclosed
by a set of 4 boxes. The size of these boxes is 2 x 2 cm. The color scale used to pseudo-color the PETT data is the 'heat scale': twelve
equal bins of data are displayed, using white, yellow, orange, red . . . blue for the pseudo-color display. Thus, the posterior region of
primary visual cortex in the left hemisphere is stimulated (top center), corresponding to the superior central right visual field stimula-
tion. This PETT section was located 4.5 cm above the cantho-meatal plane. In the higher section shown, located at 5.5 centimeters
above the cantho-meatal plane, the pattern of [^{18}F]DG labeling has shifted forwards, to an anterior position (by about 2 cm), and was
still lateralized to the left hemisphere, as shown on the top right. The asymmetries in these two sections were measured to be 10 and
40% for the central (foveal) and peripheral regions, respectively. Noticeable in this figure is the 'spillover' from left to right hemi-
sphere in the central representation (center top). This 'spillover' largely accounted for the smaller value of asymmetry observed in the
central representation of visual field. On the lower part of the top section, 3 figures are presented for the purpose of illustrating the ex-
pected 'signature' of the stimulus. On the bottom left is shown a medial view of human visual cortex[13]. The striped area represents
striate cortex, and the shaded area represents the 'signature' of the stimulus shown on the top left. Thus, the small superior central re-
gion of stimulus corresponds to the inferior posterior region shaded in yellow (bottom left), while the larger peripheral region corre-
sponds to the superior anterior cortical region shaded in yellow. Also shown are two dotted lines, parallel to the cantho-meatal plane,
which are separated by 1 cm. Bottom center and bottom right of the top section show two sections of human brain, at the approximate
cantho-meatal level of the two PETT sections shown on top. A similar indication of the mid-line and a 2 x 2 set of 'boxes' which are
each 2 x 2 cm in size, is also shown. The shaded areas in these 'boxes' correspond to the expected signature of the stimulus, later-
alized to the left hemisphere, with the central visual region mapped to the posterior, inferior cortical 'box', while the peripheral visual
region is mapped to the superior cortical 'box'. These match the observed PETT data very well. Bottom: same as above, but another
subject, and another stimulus condition. The left visual field is stimulated in the superior central and inferior peripheral regions. Cor-
responding PETT sections indicated neural activation in the appropriate regions, as illustrated in the figure.

task, which is difficult to perform consistently for the 20 min duration of stimulation used, provided some degree of control over the internal state of the subjects. Of 4 subjects tested, two could not perform this task to criterion (>80%) and were eliminated from further study. The majority of the subjects reported that the task required focused attention, and was difficult. Thus, some degree of control over subject 'set' was provided.

Subjects spent about 20 min rehearsing the stimulus letter identification task with the particular stimulus movie which they were to view during the experiment. Two movies were used: a right visual field stimulus with superior central and inferior peripheral visual field stimulation, and a left visual field stimulus, with inferior central and superior peripheral visual field stimulation (Fig. 1). These were shown in alternation to successive subjects. Following rehearsal, dark adapted subjects received 5 miC injections (i.v.) of [18F]DG. Then, a 20 min stimulation period followed, during which the subjects viewed the movie and identified the random letter presentations.

Following visual stimulation, subjects were placed in the PETT-I11 scanner. Head alignment was performed with lasers fixed with respect to the scanner gantry. Then, a series of 9 serial PETT scans were obtained, parallel to the cantho-meatal (CM) plane, starting at 2–2.5 cm above the CM plane. Head position was monitored during scanning with the same laser system used for initial set-up. PETT sections were obtained at 0.8 cm intervals (0.5 cm for one subject) over a range of 5 cm, for a total of 7 male, adult (age 20–50 years) subjects.

Image analysis was performed off-line using a computer controlled (PDP-11/23) color video display system. The images obtained from each subject were visually examined for evidence of the expected 'signature' created by the stimulus movie. Examples of this expected 'signature', the stimulus, and representative PETT data, are shown in Fig. 1. The topographic signatures expected are clearly evident in Fig. 1, in the form of an asymmetry whose CM and anterior-posterior coordinates change in the manner predicted by the topographic structure of the stimulus.

The predicted pattern of topographic and lateralized cortical stimulation (Fig. 1) was located in 6 of 7 subjects, by visual inspection of computer graphic displays of the PETT data. Quantitative analyses of this data were performed by shifting a small grid composed of four 2 x 2 cm boxes (Fig. 1) along the midline of the sections in the PETT sections in which the topographic 'signature' was observed. Using estimates of striate cortex surface area in humans[13], and mathematical models of striate cortex topography[3,11,12] the cortical representation of the stimulus was expected to consist of 4 equal sized 'patches', corresponding in size to this grid. The midline of each PETT section was found by fitting a line to the average of the geometric limits of the PETT images at anterior, central, and posterior positions. Then, the grid (Fig. 1) was shifted along this mid-line in order to provide the best fit to the expected pattern of stimulation. When the optimal grid position was found, asymmetry was calculated by dividing the difference of the ipsilateral and contralateral [18F]DG counts by their sum, in each box of the grid, for homologous areas on either side of the midline. The result of this analysis was that an average asymmetry of 15% (central) and 24% (peripheral) was found in the group of 6 subjects (see Table I).

The smaller asymmetry observed in the central (0–10°) representation of striate cortex was visually confirmed by examining the PETT data. Several of the subjects had a noticeable 'spillover' of FDG activity, in the central (but not peripheral) representation, from contralateral to ipsilateral hemispheres. The examples of data shown in Fig. 1 indicates clearly this central 'spillover' effect.

The cause of this reduced asymmetry in the central

TABLE I

The asymmetries in the region of V1

Subject VS002 had no observable effect correlated to the stimulus (NOE) The asymmetries are calculated as described in the text.

Subject	Central asymmetry	Peripheral asymmetry
VS001	11%	40%
VS002	NOE	NOE
VS003	14%	6%
VS004	29%	59%
VS005	20%	6%
VS007	12%	23%
VS009	4%	8%
Average	15%	24%

representation could be due to: (1) the bilateral presentation of the fixation letter; or (2) small errrors in eye fixation. Both of these effects would be exaggerated by the large value of cortical magnification in the central visual representation.

The topographically distributed asymmetries observed in the present experiment (15% central, 24% peripheral) may be compared with a previous experiment using PETT-III[5] which studied hemi-field stimulation, but not topographic mapping. The average asymmetry obtained in that experiment was 8%, which is similar to the central value obtained in the present experiment, but smaller than the peripheral value obtained in the present experiment. These differences may be due to the fact that the topographic aspect of the present experiment allowed a more accurate location of primary visual cortex, to the use of a cortical magnification factor scaled stimulus in the present experiment, or to differences in the eye fixation paradigms used in these experiments.

Another previous PETT experiment compared eyes-open to eyes-closed stimulus conditions, using a parafoveal checkerboard of constant size (1°). In this work, an increase in the metabolic activity of primary visual cortex of 28.8% was reported. Although the stimulus conditions and instrumentation in this experiments are not directly comparable to the present experiment, this amount of increased cortical metabolic activity is similar to the peripheral asymmetry observed in the present experiment.

In summary, the present work demonstrates that, despite the difficulties imposed by PETT technology, it is feasible to study patterns of topographic mapping in human primary visual cortex. In particular, the reasonably well understood topographic structure of primary visual cortex may be used, together with the lateralized representation of the visual field, to provide a 'signature' to verify the location of a specific architectonic area (i.e. striate cortex) in the PETT data. This is particularly important because of the complexity of the PETT images, the relative lack of experience in interpreting these images, and the difficulty in using independent means of verification (such as CAT scans) to locate specific cortical areas. This approach will be utilized with PETT-VI, which is a new scanner beginning to be used in our laboratory, which has about twice the spatial resolution of the PETT-III scanner used in the present experiment. It may be possible to obtain an approximate measurement of human cortical magnification factor by means of imaging a finer cortical 'checkerboard' pattern than the one used in the current experiment. Furthermore, the present work demonstrates that imaging cortical topography via PETT scanning provides a landmark in the visual system of individual subjects. Since a reasonable amount of variation in location of primary visual cortex was expected, and observed in the present experiment (on the order of 1–2 cm), it would seem that in order to study the stimulus preferences of human visual cortex, some form of anatomical verification is necessary. The topographic 'signature' observed in the present experiment provides one such verification.

ACKNOWLEDGEMENTS

REFERENCES

1 Allman, J. H. and Kaas, J., Representation of the visual field in striate and adjoining cortex of the owl monkey brain, *Brain Research,* 35 (1971) 89-106.

2 Dow. B. M., Snyder, A. Z., Vautin, R. G. and Bauer, R., Magnification factor and receptive field size in foveal striate cortex of monkey, *Exp. Brain Res,* 44 (1981) 213-227.

3 Drasdo, N., The neural representation of visual space, *Nature (Lond.),* 256 (1977) 554-556.

4 Gattass, R., Gross, C. G. and Sandell, J. H., Visual topography of V2 in the macaque, *J. comp. Neurol.,* 201 (1981) 519-535.

5 Greenberg, J. H., Reivich, A,, Alavi, A,, Hand, P., Rosenquist, A,, Rintelman, W., Tusa, R., Stein, A,, Dam, R., Christman, D., Fowler, J., MacGregor, R. and Wolf, A,, Metabolic mapping of functional activity in human subjects with the [18F] fluorodeoyglucose technique, *Science,* 212 (1981) 678-680.

6 Hubel, D. H. and Wiesel, T. N., Uniformity of monkey striate cortex: a parallel relationship between field size, scatter, and magnification factor, *J. comp. Neurol.,* 158 (1974) 295-302.

7 Ido, T., Wan, J. S., Fowler, J. S. and Wolf, A., Fluorination with F,, a convenient synthesis of 2-deoxy-2-fluoroglucose-o-glucose, *J. Org. Chem.,* 42 (1977) 2341-2342.

8 Mazziota, J. C., Phelps, M. E., Plummer, D. and Kuhl, D. E., Quantitation in positron emission tomography 5. physical-anatomical factors, *J. comp. Ass. Tomography,* 5 (1981) 734-740.

9 Phelps, M. E., Kuhl, D. E. and Mazziota, J. C., Metabolic mapping of the brains response to visual stimulation: Studies in humans, *Science,* 211 (1981) 1445-1447.

10 Ransom-Hogg, A. and Spillmann, L., Receptive field size in fovea and periphery of the light and dark adapted retina, *Vision Res.,* 20 (1980) 221-228.

11 Schwartz, E. L., Computational anatomy and functional architecture of striate cortex: A spatial mapping approach to perceptual coding, *Vision Res.,* 20 (1980) 645-669.

12 Schwartz, E. L., **A** quantitative model of human striate cortex, *Biol. Cybernetics,* 37 (1980) 63–76.

13 Stensaas, **S. S.,** Eddington, D. K. and Dobelle, W. H., The topography and variability of the primary visual cortex in man, *J. Neurosurgery,* 40 (1974) 747-760.

14 Tootel, R. B., Silverman, M. **S.** and de Valois, R. L., Spatial frequency columns in primary visual cortex, *Science,* 214 (1981) 813-815.

15 Tusa, R. J., Palmer, L. A. and Rosenquist, A. C., The retinotopic organization of area 17 (striate cortex) in the cat, *J. comp. Neurol.,* 177 (178) 213-236.

16 Van Essen, D. **C.** and Zeki, **S.** M., The topographic organization of rhesus monkey pre-striate cortex, *J. Physiol. (Lond.),* 277 (1978) 193-205.