Overview of the brain and of the main imaging methods

Christophe Pallier
The human brain

- Two hemispheres
- Central nuclei (including Thalamus)
- Brain stem
- Cerebellum

Volume $\sim 1400 \text{ cm}^3$ (std dev $= 250 \text{ cm}^3$).

Surface of each hemisphere (unfolded) $\sim 1\text{ m}^2$
FIGURE 7.13 — A plot of brain mass versus body mass for a variety of animals. The open circles represent reptiles (including some fish and dinosaurs), the filled circles represent mammals (including many birds), and the x's represent primates (including humans and their immediate ancestors). (Carl Sagan)
Beware: I believe the previous graphics may have been manufactured to make homo-sapiens look good.

From Wikipedia’s article « Brain-to-body mass ratio »

<table>
<thead>
<tr>
<th>Species</th>
<th>Simple brain-to body ratio (E:S)(^{[1]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>small ants</td>
<td>1:7(^{[2]})</td>
</tr>
<tr>
<td>tree shrew</td>
<td>1:10</td>
</tr>
<tr>
<td>small birds</td>
<td>1:14</td>
</tr>
<tr>
<td>human</td>
<td>1:40</td>
</tr>
<tr>
<td>mouse</td>
<td>1:40</td>
</tr>
<tr>
<td>cat</td>
<td>1:110</td>
</tr>
<tr>
<td>dog</td>
<td>1:125</td>
</tr>
<tr>
<td>squirrel</td>
<td>1:150</td>
</tr>
<tr>
<td>frog</td>
<td>1:172</td>
</tr>
<tr>
<td>lion</td>
<td>1:550</td>
</tr>
<tr>
<td>elephant</td>
<td>1:560</td>
</tr>
<tr>
<td>horse</td>
<td>1:600</td>
</tr>
<tr>
<td>shark</td>
<td>1:2496</td>
</tr>
<tr>
<td>hippopotamus</td>
<td>1:2789</td>
</tr>
</tbody>
</table>

Remarks:

- See: Olkowicz et al. (2016). “Birds Have Primate-like Numbers of Neurons in the Forebrain.” *PNAS.*
Sex Differences in Brain Gray and White Matter: Correlations with I.Q. and brain volume

(Gur et al. 1999. J. Neurosci.)

I strongly recommend to read S. J. Gould The Mismeasure of Man
The Cortex: Sulci and Gyri

Source: Ludwig & Klingler, 1956 in Tamraz & Comair, 2000
Development of Sulci

Sulci appear at predictable points in fetal development with the most prominent sulci (e.g., Sylvian fissure) appearing first.

Source: Dubois et al. (2008) Mapping the Early Cortical Folding Process in the Preterm Newborn Brain. Cerebral Cortex
SULCI on the LATERAL SURFACE of the CEREBRAL HEMISPHERE

- PRECENTRAL
- CENTRAL
- POSTCENTRAL
- SUPERIOR FRONTAL
- INFERIOR FRONTAL
- SUPERIOR TEMPORAL
- INFERIOR TEMPORAL
- INTRAPARIETAL

© 2010 PIXELATED BRAIN
Although the cortex is « continuous », neurologists divided it into **lobes**

This makes 4 lobes, but wait...
One more lobe: the **insula** (covered by temporal & frontal lobes)
The last lobe: the **limbic** lobe

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**1. Broca’s Limbic Lobe**

- Cingulate gyrus
- Olfactory bulb
- Hippocampus

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1870’s. Paul Broca

- describes a “limbic” lobe
- (limbic = border)
  - Cingulate gyrus
  - hippocampus

- Broca thought that the limbic lobe was involved in the processing of olfaction
**Grey matter** = body of neurons & dendrites.

In the **cortex**, the thickness of grey matter is \(~2-5\text{mm}\).

**White matter** = axons of neurons + glial cells (myelin)
A variety of neurons types, defined by their morphological, chemical and electrophysiological properties.

Soma size: from 4 microns to 100 microns (.1 mm).
Axon length: from a few mm to > 1m in humans (sciatic nerve)
No neuron type is specific to humans! (yet spindle neurons are only present in higher mammals)
White matter

- Nerve impulses race down axons on the order of 100 times faster when they are coated with myelin.
- Myelin is only partially formed at birth and gradually develops in different regions throughout our 20s.
- White matter was long thought to be passive tissue, but it affects how the brain learns and dysfunctions.
- Evidence for Experience-dependent changes in white-matter in Pianists.


Cortical layers and columnar organization

Drawings by Ramon y Cajal (vertical cross-sections of cortex: left: visual cortex, middle: motor cortex; right: infant's cortex)

**Columnar organization:**
Connections "up" and "down" within the thickness of the cortex are much denser than connections that spread from side to side.
Brodmann's areas (1909)

Note: cytoarchitecture by MRI not (yet?) good enough to identify Brodmann areas (BA) in vivo.
Neurons communicate using electro-chemical signals

Neurons emit **action potentials** (or spikes) (depolarisation waves) through their axons.

The change in electrical potential between the outside and the inside of the axon is due to gating of ions (K+ & Na+).

At the **synapses**, molecules called **neurotransmitters** are released and modify (+ or -) the local potential in the membrane of the postsynaptic neuron.

The post synaptic integrates the PSPs and 'decides' to emit a spike or no.
Note: the existence of electrical synapses
Vocabulary test

- Hemispheres; Cortex; Grey and white matters; Cortico-Spinal Fluid
- Lobes; Sulcus; Gyrus; Brodman Areas
- Neurons; glial cells
- Dendrites; axons; synapses; myelin
- Neurotransmitters; excitatory; inhibitory
- Action potentials (spikes and postsynaptic potentials)
Studying brain function

Classical Neuropsychology.
Symptoms ↔ Lesions

Brain of Broca's patient (Leborgne)

Geshwind (1979)'s model of repetition
A new brain region for coordinating speech articulation.
(Dronkers, 1996, Nature)

Comparison of computerized lesion overlapping in patients with and without apraxia of speech.

a, Overlapping the lesions of 25 patients with apraxia of speech yields a common area of infarction (bright yellow) in the insula.

b, Overlapping the lesions of 19 patients without apraxia of speech. Not one of these 19 patients without apraxia of speech has a lesion in the same region of the insula as those who do exhibit the disorder.

In the bottom row are shown neighbouring sections either below (section 5) or above (section 7) the critical slice.
<table>
<thead>
<tr>
<th></th>
<th>Brodmann's areas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bilateral or unilateral lesions</strong></td>
<td></td>
</tr>
<tr>
<td>Astereognosia (tactile agnosia)</td>
<td>5, 7</td>
</tr>
<tr>
<td>Visual object agnosia</td>
<td>18, 19, 20</td>
</tr>
<tr>
<td>Auditory agnosia</td>
<td>42, 22</td>
</tr>
<tr>
<td>Loss of saccadic eye movement, impaired visual search</td>
<td>8, 9</td>
</tr>
<tr>
<td>Impulsive behaviour, perseveration</td>
<td>9, 10</td>
</tr>
<tr>
<td>Changes in personality, social and sexual behaviour</td>
<td>Dorsolateral and orbital frontal cortex</td>
</tr>
<tr>
<td><strong>Left hemisphere lesions</strong></td>
<td></td>
</tr>
<tr>
<td>Colour anomia without aphasia</td>
<td>18, 19, 37</td>
</tr>
<tr>
<td>Gerstmann’s syndrome</td>
<td>7, 40</td>
</tr>
<tr>
<td>Alexia without agraphia</td>
<td>18, 19 splenium</td>
</tr>
<tr>
<td>Alexia with agraphia</td>
<td>39, 40</td>
</tr>
<tr>
<td>Agraphia without alexia</td>
<td>6 (midlateral)</td>
</tr>
<tr>
<td>Broca’s aphasia</td>
<td>6 (inferior)</td>
</tr>
<tr>
<td>Wernicke’s aphasia</td>
<td>22</td>
</tr>
<tr>
<td>Acalculia</td>
<td>18, 19, 39, 40; frontal?</td>
</tr>
<tr>
<td><strong>Right hemisphere lesions</strong></td>
<td></td>
</tr>
<tr>
<td>Constructional apraxia</td>
<td>7, 39, 40</td>
</tr>
<tr>
<td>Colour agnosia</td>
<td>18, 19</td>
</tr>
<tr>
<td>Achromatopsia (right or bilateral)</td>
<td>18, 19, 37</td>
</tr>
<tr>
<td>Prosopagnosia (right or bilateral)</td>
<td>19, 37, 20 + splenium</td>
</tr>
<tr>
<td>Contralateral neglect</td>
<td>7, 40</td>
</tr>
<tr>
<td>Anosognosia</td>
<td>5, 7</td>
</tr>
<tr>
<td>Autotopagnosia</td>
<td>7</td>
</tr>
<tr>
<td>Visual spatial agnosia</td>
<td>7, 40</td>
</tr>
<tr>
<td>Receptive amusia</td>
<td>42, 44</td>
</tr>
</tbody>
</table>
In-vivo imaging of brain functions: the main methods

Electrical activity

- Direct recordings
- Optical imaging
- Electro-encephalography (EEG)
- Magneto-encephalography (MEG)
- Transcranial magnetic stimulation (TMS)

Imaging of metabolism or blood flow

- Positron Emission Tomography (SPEC/PET)
- Nuclear Magnetic Resonance (NMR or MRI)
- Near-infrared Spectroscopy (NIRS)
Temporal and Spatial Resolutions of methods
(Huettel, Song, McCarthy; 2014, Functional Magnetic Resonance Imaging)
Recording of the activity of single neurons

Spiking activity of a neuron located in the prefrontal area when the monkey has to memorise the location of a target on the screen (delayed-response paradigm. Fuster, 1973. *J. Neurophysiol.*).
Mirror neurons (Rizzolatti, Fogassi & Gallese, 1996)

Imitation in a neonate macaque
Neurons whose activity correlates with the content of conscious perception

- During *binocular rivalry*, the monkey's perception vacillates back and forth between seeing the face and seeing the bursting sun.

The upper row indicates the visual input, with dotted vertical lines marking stimulus transitions. The second row shows the individual spikes, the third the smoothed firing rate, and the bottom row the monkey's behavior.

The monkey could control the movement of a dot on the screen either manually or mentally.

See VIDEO
Intracellular electrodes record the activity of single neurons.

Extracellular electrodes can record both the spiking activity of nearby neurons and the Local Field Potentials (LFP) which reflect the dendritic currents in a sphere of radius 0.5~3mm around the tip of the electrode.
Invasive electroencephalography in humans

Sometimes use to locate epileptic sources in the brain before surgery.

A post-implant skull X-ray showing multiple depth electrodes. In this individual, the electrodes were placed in bilateral hippocampal formations, orbitofrontal gyri and cingulate gyri.
Less invasive (but still) : Electrocorticography (ECoG)

Electrodes are put on the surface of the cortex. Spatial sensitivity ~1cm.
Single neuron recordings in humans

Activity of one neuron located in the amygdala of a patient (Kreiman, Fried, Koch, 2001)
Individual neurons are only broadly tuned to a particular direction (see Fig). Yet the precise direction of movement can be predicted by the sum of vectors associated to a population of motor cortical neurons (N=224).
Electrodes were implanted in the left precentral gyrus of a human volunteer suffering from locked-in syndrome.

Signals were transmitted wirelessly across the scalp and used to drive a speech synthesizer.

Hypothesis: neurons in left ventral premotor cortex encode desired formant frequency trajectories, which are then mapped into articulator movements in the primary motor cortex.

Result: better than chance attainment of targets vowels /a/, /i/, /u/

SEE VIDEO
Reconstructing speech from human auditory cortex.
(Pasley et al. (2012) Plos Biology)

Remark: this study used Electrocorticography (EcoG), not depth electrodes
Brain imaging methods

Electrical activity
- Direct recordings
- Electro-encephalography (EEG)
- Magneto-encephalography (MEG)
- Transcranial magnetic stimulation (TMS)

Imaging of metabolism or blood flow
- Positon Emission Tomography (SPEC/PET)
- Nuclear Magnetic Resonance (NMR or MRI)
- Near-infrared Spectroscopy (NIRS)
Electro-encephalography (EEG)

1927...

...2000

Electrodes are put on the scalp and measure an image of the electrical activity of the brain.
Awake — Low Voltage — Random, Fast

Drowsy — 8 to 12 cps — Alpha Waves

REM Sleep (D Sleep) — Low voltage — Random, Fast

Stage 1 — 3 to 7 cps — Theta Waves

Stage 2 — 12 to 14 cps — Sleep Spindles and K Complexes

Delta Sleep (S Sleep) — $\frac{1}{2}$ to 2 cps — Delta Waves
Evoked Potentials: the example of the Mismatch Negativity (MMN)

- The MMN is a passively elicited response to an acoustically different (deviant) stimulus presented in a series of homogeneous (standard) stimuli.
- It is, for example, a good predictor of coma outcome (Fisher et al. 1999, Kane et al. 2000).
The time course of auditory perceptual learning: neurophysiological changes during speech-sound training (Tremblay, Kraus, McGee, 1998, Neuroreport)

- Ten participants were trained, over a period of ten days, to distinguish between two instances of /ba/ differing in acoustically (Voice onset time)
ERP to incongruent or unexpected words (Kutas & Hillyard, 1980)

Event-Related Potentials (ERP)
Data acquisition

Remark: What is wrong on this picture?
Electrodes naming scheme
ERP conventional data analysis

- Temporal Filtering (bandpass and 50 or 60Hz)
- Artifact detection and rejection (e.g. eye movements)
- Segmentation at event onsets and averaging, within subject
- Statistical testing within or across subjects
Artifact detection and rejection
Averaging
1) At each time-point, perform a statistical test (t or F-test) at a given $\alpha$ threshold.
2) Compute the length of runs reaching the threshold.
3) Compare them to run length in randomly generated signal having the same autocorrelation.
(one issue is properly estimating the autocorrelation)
Time-frequency analysis

Wavelet transform

$S(t)$

$W_f(s, \tau) = \int_{-\infty}^{\infty} f(t)h^*_\tau dt$

helpful representation both in time and in frequency.

$f = 25$ Hz

$t = 50$ ms

Table 1. Example Stimuli in Each Condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>Example Stimulus</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: COR</td>
<td>Janneke kreeg de <em>zegen</em> bij de rivier.</td>
</tr>
<tr>
<td></td>
<td>(<em>Janneke got the blessing at the river</em>).</td>
</tr>
<tr>
<td>B: CAT</td>
<td>Janneke kreeg de <em>zegenen</em> bij de rivier.</td>
</tr>
<tr>
<td></td>
<td>(<em>Janneke got the “to bless” at the river</em>).</td>
</tr>
<tr>
<td>C: RDM</td>
<td>De de Janneke <em>zegen</em> kreeg rivier bij.</td>
</tr>
<tr>
<td></td>
<td>(<em>The the Janneke blessing got river at</em>).</td>
</tr>
</tbody>
</table>

Literal English translation in italics.
Main limit of EEG: spatial resolution

The electric field is very much deformed by the skull and it is nearly impossible to infer the spatial origin(s) of the signal within the brain.

Remember, in **electrocorticography** (EcoG), electrodes are placed directly on the exposed surface of the brain. ECoG offers a temporal resolution of approximately 5 ms and a spatial resolution of 1 cm (to be compared with depth electrodes which have a spatial resolution of 0.5-3 mm).
Source localization in EEG

- Idea: try to find electrical dipoles that generate the electric field measured on the scalp.

This is called an 'inverse problem'. It is difficult because an infinite number of solutions exists, and the noise in the data make unstable the prediction.
“Brain computer interface” (BCI) with EEG

- 2000: Brain Pong (MOVIE)
- 2008: commercial headset for gamers
Magneto-encephalography (MEG)

Electric currents (moving electric charges) generates magnetic fields

Units: Tesla or Gauss: $1 \text{T} = 10^4 \text{G}$

Earth magnetic field: $0.5 \text{G} = 5 \times 10^{-5} \text{T}$, Small bar magnet: $100 \text{G} = 0.01 \text{T}$, Big electromagnet: $10000 \text{G} = 1 \text{T}$
EEG measures voltage differences across the scalp.

MEG measures the magnetic field engendered by currents.

The magnetic field is detected by supraconductors (conductors without resistance).
Both in EEG and MEG, the primary source of the signal is the current flow in the apical dendrites of pyramidal cells in layers 3-6 of the cerebral cortex.
Differences between EEG and MEG

- MEG is particularly sensitive to tangential dipoles, parallel to the scalp and less to the radial ones. It is the opposite for EEG.

- As the magnetic field is less distorted by the skull, the localisation of sources of activity is much better in MEG than in EEG.

See https://www.youtube.com/watch?v=Uxr5Pz7JPrs
Magnetic source imaging revealed that the cortical representation of the digits of the left hand of string players was larger than that in controls. The amount of cortical reorganization was correlated with the age at which the person had begun to play.

Fig. 1. (A) Equivalent current dipoles elicited by stimulation of the thumb (D1) and fifth finger (D5) of the left hand are superimposed onto an MRI (magnetic resonance imaging) reconstruction of the cerebral cortex of a control, who was selected to provide anatomical landmarks for the interpretation of the MEG-based localization. The arrows represent the location and orientation of the ECD vector for each of the two digits averaged across musicians (black) and controls (yellow). The length of the arrows represents the mean magnitude of the dipole moment for the two digits in each group. The average locations of D5 and D1 are shifted medially for the string players compared to controls; the shift is larger for D5 than for D1. The dipole moment is also larger for the musicians’ D5, as indicated by the greater magnitude of the black arrow. (B) The magnitude of the dipole moment as a function of the age of inception of musical practice; string players are indicated by filled circles, control subjects by hatched circles. Note the larger dipole moment for individuals beginning musical practice before the age of 12. (C) Scatterplot of the Euclidean distances (in centimeters) between the cortical representations of D1 and D5. This distance for the musicians’ left hands was greater than that in controls, but this difference is not statistically significant.
Auditory evoked responses
(Schneider et al. 2002. *Nature Neurosci.*)

Non-musicians, professional musicians and amateurs were scanned with MEG (response to pure tones) and structural MRI.

Results: differences in the magnetic field component (N19m-P30m).

Anatomical differences in HG morphology with differences in musical aptitude.
Pro and Cons

• Both techniques have a high temporal resolution (signal can be sampled every msec)

• MEG permits a much better localization of sources because the magnetic field is less distorted than the electric field by the skull.

See https://www.youtube.com/watch?v=Uxr5Pz7JPrs

• EGG is much cheaper than MEG
Transcranial magnetic stimulation (TMS)
Seeing and hearing speech excites the motor system involved in speech production (Watkins, Strafella, Paus, 2003, Neuropsychologia)

Fig. 1. Experimental set-up and typical MEP data. The upper half of the figure is a schematic showing the position and orientation of the stimulating coil and the placements of recording electrodes on the contralateral orbicularis oris muscle. The drawing of the head with face muscles is adapted from [19]. The lower half of the figure shows data from stimulation of the left primary motor face area in a single subject in each of the four experimental conditions. EMG recordings from individual trials are superimposed. The dotted line represents the time of stimulation. The horizontal bar represents 10ms and the vertical bar 0.5mV.
Brain imaging methods

Electrical activity
- Direct recordings
- Electroencephalography (EEG)
- Magnétoencephalography (MEG)

Imaging of metabolism or blood flow
- Positon Emission Tomography (PET scan)
- Near-infrared Spectroscopy (NIRS)
  Nuclear Magnetic Resonance (NMR or MRI)
The fuels of the cells are **oxygene** and **glucose**.

Increases of neuronal activity leads to increased consumptions of glucosis and oxygene.

The cerebral metabolic rates of glucose (CMRglu) and oxygene (CMRO2) are markers of neural activity.
The brain is not only a « blood-cooler »:
The energy budget of the (rodent) brain
(Attwell & Laughlin ; 2012)
Positron Emission Tomography (PET)

- A molecule marked with radioactivity (a « radiotracer ») is injected in the blood stream
- the desintegration events can be tracked by cameras.
- In PET, a **positon** is emitted, that will produce 2 high energy photons when encountering an electron
Figure 1 Positron emission tomography (PET) imaging. Until the mid-1990s, the most common functional neuroimaging technique was PET, which relies on the injection of a radioactive tracer into the bloodstream. As the tracer decays, it emits positrons, which travel a short distance before colliding with an electron (A). The collision results in a pair of emitted gamma rays that travel in opposite directions. The PET scanner (B) consists of a series of coincidence detectors that record the simultaneous arrival of these gamma rays. Depending on the tracer used, PET can be sensitive to several aspects of brain metabolism, including blood flow or oxygen consumption. The output of a PET scan indicates the number of events measured from each voxel during a long time period. (C) These numbers can be converted to statistical maps, which can then be overlaid on anatomical images, often from MRI. (C courtesy of Dr. David Madden, Duke University.)
Regional metabolism using FDG-PET

- Glucose provides approximately 95-99% of the brain’s energy requirement under normal conditions, and the rate at which glucose is utilized in different regions of the brain is an excellent indicator of local energy-requiring functions.
- Radiolabeled glucose: (fluoro-2-deoxyglucose, or FDG).
- Half life of FDG = 2 hours.

Whole body FDG-PET of a normal volunteer:
H$_2$O$^{15}$ PET experiment

- Regional **cerebral blood flow (rCBF)** is tightly coupled to cortical metabolism of glucose (**CMRglu**).

- A typical experiment consists of 12 runs of 90 seconds each, separated by 8~10 minutes.

- Result = 12 scans with a spatial resolution around 8x8x8 millimeters

- In comparison, a typical fMRI experiment can yield more 3000 scans with a 2x2x2mm resolution, in less than one hour.
Positron emission tomographic studies of the processing of single words. Petersen et al. (1989) *J. Cognitive Neuroscience*
Nowadays, PET is less used for cognitive studies, yet...

- Assessment of metabolism in deaf subjects before cochlear implementation (Lee et al, *Nature*, 2001)

- The intelligibility scores 2 years after implantation correlate with hypometabolism in language regions.

![Diagram showing the relationship between duration of deafness and CID scores.](image)
Diffuse optical imaging. NIRS

- Changes in neural activity **indirectly** alter the local concentrations of oxyhemoglobin (carrying $O_2$) and deoxyhemoglobin.

- By measuring the absorption of light at precise wavelengths, it is possible to follow changes in oxyhemoglobin and deoxyhemoglobin concentration.
Diffuse optical imaging in infants

Fourteen neonates ranging in age from 2 to 5 days (mean age 2.7 days) listened to normal speech (red), temporally reversed speech (blue) or silence (green).

Results:
LH temporal areas showed significantly more activation when infants were exposed to normal speech than to backward speech or silence.
Magnetic Resonance Imaging (MRI)
(used to be called 'Nuclear Magnetic Resonance' or MNR)
Magnetic Resonance Imaging (MRI) 
(used to be called 'Nuclear Magnetic Resonance' or NMR)

Timeline for RMN
1940s: Discovery of the Nuclear Magnetic Resonance phenomenon (Bloch & Purcell, Nobel prize in physics 1952)
1973: Imaging with NMR (Lauterbur & Mansfield: nobel prize in medicine 2003)
1992: functional MRI (Ogawa & Kwong)
1985-1995: Invention of diffusion MRI (DTI)
3 examples of applications
An Effect of Bilingualism on the Auditory Cortex  
(Ressel et al. 2012, *J. Neurosci.*)

Comparison of the volumes of Heschl Gyri (Auditory cortex) in 22 Spanish monolinguals and 22 Spanish Catalan bilinguals.

Figure 1. Distributions of individual Heschl’s gyrus volumes (in mm$^3$; normalized space) as a function of Side (left vs right hemisphere) and Group (monolingual vs bilingual). Left, Each line represents one Heschl’s gyrus for each participant. The distribution of the volumes, the mean, and the SE are shown. Right, Probability maps of Heschl’s gyrus.
Brain areas more activated when listening one’s maternal language than to unknown foreign languages

(single participant; threshold: p<0.05 FWE corrected)
Diffusion Tensor Imaging (DTI)

Visualization of DTI data with ellipsoids (Wikipedia)

Result of a « fiber-tracking » algorithm
The evolution of the arcuate fasciculus revealed with comparative DTI
(Rilling, Glasser, Preuss, Ma, Zhao, Hu, Behrens, 2008, Nature Neuroscience)

« The cortical terminations of humans differed from chimpanzees and macaques, with humans having much stronger terminations posteriorly, in the MTG and ITG, as well as anteriorly, in pars opercularis, (BA 44), pars triangularis (BA 45), pars orbitalis (BA 47) and surrounding regions »