Reciprocal Thalamocortical Connectivity of the Medial Pulvinar: A Depth Stimulation and Evoked Potential Study in Human Brain

The thalamic medial pulvinar nucleus (PuM) is fully developed only in primates and reaches its greatest extent in humans. To assess the reciprocal functional connectivity between PuM and cortex, we studied intracerebral-evoked responses obtained after PuM and cortical electrical stimulation in 7 epileptic patients undergoing depth electroencephalographic recordings. Cortical-evoked potentials (CEPs) to PuM stimulation were recorded from all explored cortical regions, except striate cortex, anterior cingulated, and postcentral gyrus. Percentages of cortical contacts pairs responding to PuM stimulation (CEPs response rate) ranged from 80% in temporal neocortex, temporoparietal (TP) junction, insula, and frontoparietal opercular cortex to 34% in mesial temporal regions. Reciprocally, PuM-evoked potentials (PEPs) response rates were 14% after cortical stimulation in insula and frontoparietal opercular cortex, 67% in the TP junction, 76% in temporal neocortex, and 80% in mesial temporal regions. Overall, our study of functional PuM connectivity in the human brain converges with most of the data from anatomical studies in monkeys, except for a strong amygdalo-hippocampal functional projection to PuM and an unexpected imbalance between some of the reciprocal pathways explored. This functional quantitative approach helps to clarify the functional role of PuM as well as its implication in temporal lobe epileptic seizures.

Keywords: epilepsy, evoked potentials, functional connectivity, human medial pulvinar, thalamocortical pathways

Introduction

To date, most of our knowledge of thalamocortical connectivity derives from animal studies, raising a difficulty when extrapolation to human brain is at stake. In humans, anatomical studies rely on postmortem injections of fluorescent dyes that allow the tracking of some projections but only at distances of tens of millimeters from the injected area (Mufson et al. 1990; Lim et al. 1997; Tardif and Clarke 2001; Tardif et al. 2007). Additional information comes from gross dissections or from histological studies of remote degeneration following a focal lesion, which are based on a small number of patients (Clarke et al. 1999). Recently, diffusion tensor magnetic resonance tractography has enabled in vivo tracing of large fiber tracts in the human brain and has been applied to visualize the major thalamocortical fiber bundles (Behrens et al. 2003). However, this technique does not provide with details about the functionality of these tracts and their conduction velocity and is unable to distinguish thalamocortical from reciprocal corticothalamic connections. Some authors have attempted to use transcranial magnetic stimulation and scalp recordings to assess the functional corticothalamic connectivity, but this method has a spatial resolution limited to the cortex and cannot be applied to the study of thalamocortical connections (Rossini and Rossi 2007).

Recently, the electrophysiological study of subcortical structures, in particular the thalamus, has known a revival in epilepsy because of growing evidence that they are involved in propagation and synchronization of epileptic discharges (Bertasthius 1991; Szabo et al. 2005; Guye et al. 2006). On this line, we have shown that the thalamic medial pulvinar nucleus (PuM) is involved in most of temporal and insular lobe seizures (Rosenberg et al. 2006). Because recent attempts to control epileptic seizures by chronically stimulating thalamic nuclei have led to some encouraging results (Velasco et al. 2006; Andrade et al. 2006), we decided to investigate whether chronic PuM stimulation could represent an alternative treatment for patients with drug-resistant epileptic seizures who are not eligible for surgical resection of the epileptogenic zone. In this context, a precise knowledge of the thalamocortical and corticothalamic functional connectivity is crucial to define the cortical territories that could be functionally influenced by this therapeutic approach. Our present knowledge of PuM connectivity is mostly based on anatomical studies in monkeys, which suggested widespread reciprocal connections between PuM and temporal, parietal, frontal, and occipital cortical areas (Trojanowski and Jacobson 1977; Robinson and Cowie 1997; Romanski et al. 1997; Grieve et al. 2000; Gutierrez et al. 2000). However, PuM is in humans the thalamic structure showing the greatest phylogenetic expansion as compared with nonhuman primates and, consequently, the most susceptible to show anatomical variations as compared with other animal species. It was thus essential to reevaluate PuM connectivity in humans. For this purpose, we used electrical stimulations coupled with intracerebral recordings of evoked responses in epileptic patients chronically implanted with depth electrodes for stereoelectroencephalographic (SEEG) assessment of their epileptic focus. Furthermore, we attempted to estimate quantitatively the preferential pathways between the cortex and PuM using the same approach as that recently proposed by Matsumoto et al. (2004, 2007).

Materials and Methods

Patients

Seven patients, 4 women and 3 men, aged 34 ± 9.6 years (range = 16-47), were included in this study (Table 1). They were suffering from drug-resistant partial epilepsy suspected to originate from the temporal lobe. All patients were referred to the Epilepsy department of the Neurological Hospital in Lyon for SEEG recording of their seizures because noninvasive presurgical investigations had not permitted to delineate their epileptogenic zone precisely enough to plan a surgical...
cortectomy and in particular a standard temporal lobectomy. All
patients were included in the phase 1 of a protocol designed to
evaluate the feasibility of chronic PuM stimulation as a treatment for
temporal lobe epilepsy (TLE). Noninvasive presurgical data included
scalp videoelectroencephalographic monitoring of seizures, brain
magnetic resonance imaging (MRI), interictal and ictal single-photon
emission tomography, and 18F-fluorodeoxyglucose positron emission
tomography (FDG-PET).

Stereotactic Implantation of Deep Brain Electrodes

Determination of SEEG Cortical Targets

The cortical regions to be explored as well as the number of electrodes
were individually determined for each patient, based on individual
presurgical data. Nine to 13 multiple contacts electrodes were
implanted per patient. Four implantations were performed in the left
hemisphere and 3 in the right one.

PuM Implantation and Recordings

PuM stimulation and/or recording were performed using the 2–4
deepest contacts of the electrode exploring the posterior part of the
superior temporal gyrus (see Rosenberg et al. 2006). Therefore, no
electrode was specifically implanted to record the thalamus in addition
to those required by the diagnostic SEEG procedure. All patients were
fully informed of the aim of this investigation and gave their written
consent about the implantation and stimulation procedure, which was
approved by the local ethics committee (CCPPRB Lyon—Centre Léon
Bérard).

Stereotactic Implantation Technique

Intracerebral exploration was conducted according to the technique
described by Talairach and Bancaud (1973), a procedure used routinely
in our department (Guenot et al. 2001). Intracerebral electrodes were
implanted perpendicular to the midsagittal plane (Fig. 1A) and could be
left in place for 15 days. The electrodes had a diameter of 0.8 mm and
were implanted perpendicularly to the midsagittal plane (Fig. 1A) and could be
left in place for 15 days. The electrodes had a diameter of 0.8 mm and
were separated by 1.5 mm one

Localization Checking of the Recording Contacts

To verify the final position of each implanted contact with respect to
the targeted anatomical structures, frontal and sagittal X-rays at scale 1
were obtained at the end of the surgical procedure, using an X-ray
source at 4.85 meters from the patient’s head thus eliminating the
linear enlargement due to X-ray divergence. The T1-weighted MRI
midsagittal slice was superimposed on the sagittal X-ray, after
enlargement at scale 1 using the limits of the cranial bone as a common
reference. This allowed to define the position of the anterior
commissures (AC) and posterior commissures (PC) and to calculate
the anteroposterior and dorsoventral coordinates of each electrode
contact. The mediolateral coordinate of each contact was determined
on the frontal X-ray with respect to the midsagittal plane. Each contact
was then localized in the Talairach space (Talairach and
Tournoux 1988) according to 3 coordinates in millimeters: x for the
distance from the interhemispheric sagittal vertical plane, y for the
distance from the coronal plane perpendicular to the horizontal AC–PC
plane passing through PC, and z for the distance from horizontal AC–PC
plane. In this reference system, the coordinates of the PC midline point
serves as reference with x = y = z = 0. The 3-dimensional (3-D)
position of all contacts within cerebral structures in a given patient was
checked by plotting their coordinates in the patient’s MRI volume (T1-
weighted images, 1-mm based voxel) reconstructed in the 3-D space
using Mricro Software (Rorden and Brett 2000; Fig. 1B).

This method is based on measurement of coordinates in the
Talairach’s stereotaxic space and not on direct MRI visualization of
contacts after electrodes implantation. Therefore, even after correction
for contacts locations and evaluation of PuM limits based on individual
patient’s MRI (Fig. 1), the contact localization in anteroposterior and
dorsoventral dimensions is prone to several inaccuracies linked to MRI
slice thickness (±0.5 mm), superimposition of MRI slice on X-ray (±1
mm), and coordinates measurement (±0.5 mm), which leads to an
average error (square root of the sum of the squares of the different
errors) of ±1.32 mm. In the mediolateral dimension, inaccuracies are
limited to the determination of the midsagittal plane on X-ray (±1 mm)
and coordinates measurement (±0.5 mm) leading to an average error
of 1.11 mm. Combined together, these error values lead to a mean
Euclidean error of 2.17 mm in the 3-D space.

The localization of the PuM contacts was checked by writing out
their coordinates on corresponding planes of a stereotactic atlas of the
human thalamus (Morel et al. 1997; Fig. 1B–D). Anteroposterior
coordinates of thalamic electrodes ranged from 0 to −7.5 mm caudal
to PC and dorsoventral ones from +2 to +6 mm above the horizontal
AC–PC plane. The x coordinates of the medialmost PuM contacts of the
electrodes were 7–10 mm lateral to the interhemispheric vertical
plane. Furthermore, we checked that none of PuM contacts could be
located outside this structure taking into account the mean Euclidean
e error of 2.17 mm in contact localization. As illustrated in Figure 1C, this
was achieved for all contacts except for the most medial one in patient
7, the deepest edge of which was at a distance of 1.6 mm from the
medial PuM border so that the inner part of this 2-mm contact may
have been out of the thalamus border. The number of contact pairs
situated inside the PuM in each patient is given in Table 1.

Finally, we checked that all of the contact pairs used for cortical
recording and stimulation were located in the cortical gray matter (see
Supplementary Materials). Each contact was plotted in the patient 3-D
MRI using Mricro software, and the implanted structure was identified
using Duvernois (1991) and Ono et al. (1990) atlases.

Stimulation Parameters

Square pulses of current were applied between 2 adjacent contacts
(bipolar stimulation), delivered by a current-regulated stimulator
approved for use in human subjects (IRE 600 CH Surgical, Micromed,
Italy). Stimulation parameters were chosen to avoid tissue damage
(Gordon et al. 1990) and were similar to those previously used in
human studies (Wilson et al. 1990; Valentin et al. 2002; Catenoix et al.
2005; Zumsteg, Lozano, and Wennberg 2006; Zumsteg, Lozano, Wieser,
and Wennberg 2006; Lacruz et al. 2007). They consisted of 2 series of

Table 1
Individual clinical, MRI, and SEEG data

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Epilepsy duration (years)</th>
<th>MRI</th>
<th>Seizure onset zone determined by SEEG procedure</th>
<th>Number of electrodes</th>
<th>Number of tested cortical contact pairs</th>
<th>Number of tested PuM contact pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>F</td>
<td>10</td>
<td></td>
<td>Hypersignal on left and right temporal pole</td>
<td>11</td>
<td>47</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>47</td>
<td>M</td>
<td>17</td>
<td></td>
<td>Normal</td>
<td>11</td>
<td>41</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>F</td>
<td>24</td>
<td></td>
<td>Right hippocampal sclerosis</td>
<td>12</td>
<td>57</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>F</td>
<td>27</td>
<td></td>
<td>Bilateral heterotopias</td>
<td>13</td>
<td>59</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>F</td>
<td>14</td>
<td></td>
<td>Normal</td>
<td>9</td>
<td>41</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>M</td>
<td>23</td>
<td></td>
<td>Left amygdala hypersignal</td>
<td>10</td>
<td>46</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>M</td>
<td>20</td>
<td></td>
<td>Normal</td>
<td>10</td>
<td>38</td>
<td>3</td>
</tr>
</tbody>
</table>
mentioned that other factors might have a nonnegligible influence on stimulation efficacy including fibers electrophysiological properties (un- or myelinated axons, chronaxy) (Ranck 1981), orientations of the neuronal elements relative to the electrodes (Manola et al. 2007), and conductance differences between white and gray matters, which cannot be controlled in our experimental conditions. Taking into account all of these considerations, we estimate that the maximal tissue volume stimulated in our conditions is that of a sphere with a 4-mm radius.

The most medial PuM contacts pair was used for thalamic stimulation in all patients. Given their large number, it was not possible to stimulate all cortical contact pairs. Therefore, we selected for stimulation 1–3 contact pairs per patient in each of the implanted cortical regions. A detailed list of studied cerebral regions is given in Table 2. Cortical stimulation was performed on the same day as, or eventually the day after, PuM stimulation. None of the patients experienced any clinical sensation resulting from cortical or PuM stimulations.

Data Collection and Analysis

Signals were recorded through bipolar derivation between 2 adjacent contacts located either in the cortical gray matter or in PuM using a hand-pass filter of 0.3–200 Hz and a sampling frequency of 512 Hz, which allowed a time resolution of 2 ms. Averaging of responses to each series of 25 stimuli was performed off-line using a time window of 4.5 s, with 500-ms pre- and post-stimulus periods. Cortical responses to PuM stimulations were named cortico-evoked potentials (CEPs) and PuM responses to cortical stimulations were named pulvinar-evoked potentials (PEPs). They were analyzed on bipolar recordings between 2 adjacent contacts in all cases. To be considered present, CEPs and PEPs should fulfill 2 conditions (Fig. 2): reproducibility between 2 consecutive series and amplitude at least twice that of the background level.

Responses evoked by intracerebral stimulation can theoretically result either from orthodromic or antidromic inputs transmission along connecting pathways, so that they can reflect either feed forward transmission to the recorded area or feed back transmission from the stimulated area. It is generally accepted that the initial segment of axons is the most excitable element recruited by electrical stimulation (Rattay 1999) and that responses evoked by electrical stimulation reflect mainly postsynaptic potentials resulting from indirect mono or polysynaptic cell activation (Jankowska et al. 1975). Therefore, the responses we recorded are likely to reflect orthodromic transmission. Even though the possibility of retrograde transmission cannot be definitely ruled out, we considered CEPs as reflecting activation of thalamocortical pathways and PEPs as resulting from activation of reciprocal corticothalamic connections.

Thalamocortical functional connection for a given cortical region was estimated by calculating the percentage of cortical contact pairs showing CEPs after PuM stimulation, with respect to the total number of contact pairs exploring this region (see Fig. 2 and legend). The reciprocal pathway was quantitatively evaluated by the percentage of stimulated contact pairs inside a given cortical area, which were able to elicit PEPs. PEPs were considered present when observed on at least one bipolar derivation inside PuM. In the majority of cases, PEPs were either absent or recorded on all PuM contacts pairs.

CEPs latencies were measured from the onset of their ascending slope (onset latencies). Maximal amplitudes and responses duration were also considered, and we attempted to classify responses according to their morphology.

Finally, to evaluate the potential influence of epilepsy on the EPs, we reviewed all the seizures recorded in each individual patient and determined the seizure onset zone, defined as the cerebral regions exhibiting the earliest ictal activities. All bipolar derivations involved during the first second of the epileptic discharge were considered located inside the seizure onset zone and then labeled epileptic derivations.
Results

Global Connectivity

An overview of cortical–PuM connectivity is given in Figure 3. Furthermore, localizations of CEPs and PEPs in each cerebral structure and for each exploring contact pairs are presented on individual patient MRI slices as Supplementary Material. None of the single-shock stimuli delivered to the cortex or PuM for EP recordings produced any clinically detectable response nor any subjective somatosensory, visual, or auditory sensation. PuM stimulation evoked CEPs in all explored cerebral regions except the anterior cingulate gyrus (2 patients), the striate cortex (2 patients), and the postcentral gyrus (1 patient). PEPs were also recorded after stimulation of all investigated cortical structures.

Table 2

<table>
<thead>
<tr>
<th>CEP</th>
<th>Number of tested patients</th>
<th>Number of responding patients</th>
<th>Number of tested contact pairs</th>
<th>Response rate</th>
<th>Onset latency (mean ± SD) (ms)</th>
<th>PEPs</th>
<th>Number of tested patients</th>
<th>Number of responding patients</th>
<th>Number of tested contact pairs</th>
<th>Response rate</th>
<th>Onset latency (mean ± SD) (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STG (BA 22)</td>
<td>7</td>
<td>6</td>
<td>37</td>
<td>95%</td>
<td>11.4 ± 2.6</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>100%</td>
<td>56.8 ± 32.6</td>
<td></td>
</tr>
<tr>
<td>MTG (BA 21, 37)</td>
<td>7</td>
<td>6</td>
<td>50</td>
<td>70%</td>
<td>13.7 ± 2.7</td>
<td>6</td>
<td>6</td>
<td>14</td>
<td>71%</td>
<td>56.8 ± 48.4</td>
<td></td>
</tr>
<tr>
<td>ITG (BA 20, 37)</td>
<td>7</td>
<td>6</td>
<td>27</td>
<td>70%</td>
<td>16.9 ± 7.3</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>50%</td>
<td>25.4 ± 18.6</td>
<td></td>
</tr>
<tr>
<td>FG (BA 36)</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>80%</td>
<td>37.1 ± 7.6</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>50%</td>
<td>11.72 (1 patient)</td>
<td></td>
</tr>
<tr>
<td>Temporal neocortex</td>
<td>119</td>
<td>119</td>
<td>80%</td>
<td></td>
<td></td>
<td>29</td>
<td>76%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hippocampus</td>
<td>7</td>
<td>2</td>
<td>19</td>
<td>16%</td>
<td>23.3 ± 5.5</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td>83%</td>
<td>27.8 ± 7.4</td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>5</td>
<td>1</td>
<td>15</td>
<td>20%</td>
<td>60.5 (1 patient)</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>100%</td>
<td>46.9 ± 7</td>
<td></td>
</tr>
<tr>
<td>Temporal Pole (BA 38)</td>
<td>5</td>
<td>3</td>
<td>15</td>
<td>47%</td>
<td>66.4 ± 52</td>
<td>6</td>
<td>3</td>
<td>6</td>
<td>50%</td>
<td>33.2 ± 7.8</td>
<td></td>
</tr>
<tr>
<td>Parahipp Gyr (BA 28, 34, 35)</td>
<td>6</td>
<td>3</td>
<td>12</td>
<td>67%</td>
<td>71 ± 47.3</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>100%</td>
<td>43.5 ± 28.2</td>
<td></td>
</tr>
<tr>
<td>Mesial temporal structures</td>
<td>61</td>
<td>34</td>
<td>34%</td>
<td></td>
<td></td>
<td>20</td>
<td>80%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus (BA 3, 2, 1)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0%</td>
<td>NA</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>TP Junction (BA 39, 40)</td>
<td>7</td>
<td>5</td>
<td>21</td>
<td>81%</td>
<td>15.2 ± 4.9</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>67%</td>
<td>23.4 ± 2.8</td>
<td></td>
</tr>
<tr>
<td>Precuneus (BA 7)</td>
<td>4</td>
<td>3</td>
<td>11</td>
<td>46%</td>
<td>29.3 ± 19.8</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>61</td>
<td>61</td>
<td>61%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insula</td>
<td>6</td>
<td>6</td>
<td>16</td>
<td>94%</td>
<td>17 ± 6.7</td>
<td>5</td>
<td>1</td>
<td>6</td>
<td>17%</td>
<td>41 (1 patient)</td>
<td></td>
</tr>
<tr>
<td>FP operculum</td>
<td>4</td>
<td>4</td>
<td>13</td>
<td>85%</td>
<td>27.8 ± 16.1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Insuloopercular cortex</td>
<td>29</td>
<td>90%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cing ant gyr (BA 24, 32)</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>0%</td>
<td>NA</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Cing post gyr (BA 23, 31)</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>67%</td>
<td>17.5 (1 patient)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>100%</td>
<td>82.7 ± 11.9</td>
<td></td>
</tr>
<tr>
<td>Cingulate Gyrus</td>
<td>61</td>
<td>61</td>
<td>61%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F1, F2 gyr (BA 9, 10, 46)</td>
<td>3</td>
<td>3</td>
<td>14</td>
<td>57%</td>
<td>30.6 ± 8.8</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>33%</td>
<td>43 (1 patient)</td>
<td></td>
</tr>
<tr>
<td>Orbital gyr (BA 11, 12, 47)</td>
<td>2</td>
<td>2</td>
<td>11</td>
<td>45%</td>
<td>48.9 ± 13.8</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Frontal cortex</td>
<td>25</td>
<td>25</td>
<td>52%</td>
<td></td>
<td></td>
<td>6</td>
<td>17%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Striate cortex (BA 17)</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>0%</td>
<td>NA</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Int occ cxt except area 17 (BA 18, 19)</td>
<td>3</td>
<td>3</td>
<td>13</td>
<td>46%</td>
<td>38.4 ± 13.3</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>25%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Ext occipital cxt (BA 18, 19)</td>
<td>4</td>
<td>3</td>
<td>12</td>
<td>58%</td>
<td>18.9 ± 4.51</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>33%</td>
<td>37.1 (1 patient)</td>
<td></td>
</tr>
<tr>
<td>Occipital cortex</td>
<td>30</td>
<td>30</td>
<td>43%</td>
<td></td>
<td></td>
<td>8</td>
<td>25%</td>
<td></td>
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</tbody>
</table>

Note: The averaged response rates (number in bold) are calculated from the whole responding contacts pairs divide by the sum of all tested contacts pairs in the 7 patients, for the lobe or the cerebral structure considered. NA, nonavailable; STG, MTG, and ITG, superior, middle, and inferior temporal gyrus; FG, fusiform gyrus; Parahipp gyr, parahippocampal gyrus; TP junction, temporoparietal junction (including angular and supramarginal gyrus); FP, frontoparietal; F1 and F2, superior and middle frontal gyrus; Int occ and ext occ cxt, internal occipital and external occipital cortex; BA, Brodmann area; cing ant gyr, cingulate anterior gyrus; cing post gyr, cingulate posterior gyrus.

Figure 2. Example of CEPs recording from the mesial part of the superior frontal gyrus (F1) and from the middle frontal gyrus (F2) in patient number 7. Black and gray traces correspond to the 2 averaged responses of 2 series of 25 single-pulse low-frequency stimulations. Localization of the recording contact pairs (black ellipses) are plotted on the patient’s MfRI coronal and sagittal slices and on a normalized surface-rendering brain image (see legend of Fig. 3). Pairs 2–3, 9–10, 10–11, and 11–12 (filled ellipses) recorded significant CEPs, whereas no responses were observed from the remaining contacts pairs (pairs 1–2 and 12–13 that are represented as empty ellipses). CEPs were thus considered present in 4 out of 6 contact pairs, giving a response rate of 67%. Note that EPs morphology could vary from one pair to the other, even when contact pairs are adjacent (see 9–10 and 10–11).
regions, except the dorsolateral frontal lobe (2 patients), the orbital cortex (2 patients), the anterior cingulate gyrus (1 patient), the frontal operculum (1 patient), and the striate cortex (1 patient). Thus, only 2 regions, the anterior cingulate gyrus and the striate cortex, did not exhibit either CEPs or PEPs. PEPs after postcentral gyrus stimulation were not tested.

**Temporal–PuM Connections**

Because the epileptogenic zone was suspected to be of temporal origin in all patients, the temporal lobe was the most extensively explored region (119 contacts pairs in the temporal neocortex, mean ± standard deviation [SD] = 17 ± 5.7 per patient, and 61 contacts pairs in the mesiotemporal structures, mean ± SD = 8.7 ± 2.9 per patient). We analyzed separately results obtained in: 1) the neocortical regions, namely the superior, middle, inferior, and fusiform temporal gyrus and 2) the mesial temporal region, that is, the hippocampus, the amygdala, the parahippocampal gyrus including entorhinal cortex and the temporal pole. Data collected for each particular structure are given in Table 2.

CEPs were recorded from 78% of the contacts pairs located in the temporal neocortex, and PEPs were elicited by stimulation of 76% of the neocortical contacts pairs stimulated. STG showed the highest percentage of reciprocal functional connection with PuM. In all, 95% of the STG contacts pairs exhibited CEPs after PuM stimulation and 100% of the STG stimulations induced PEPs. Distribution and percentages of responses were approximately similar in all patients except one, in whom CEPs were totally absent and cortical stimulations could not be performed.

The results obtained in the mesial temporal region were strikingly different. Indeed, CEPs were recorded from only 34% of the 61 tested contacts pairs, with large variations across structures. For example, the largest number of contact pairs

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**Figure 3.** Overview of global PuM-cortex connectivity. All patients’ data were plotted on normalized $T_1$ MRI brain images. For each patient, all recording electrode contacts were reconstructed on their individual 3-D $T_1$ MRI volume using MRICro software. Then all contacts were saved as a region of interest (ROI) in an analyzed format. Right implantations were flipped on the left side. In a next step, each anatomical image was normalized to the standard $T_1$ MNI template using SPM2 (Wellcome Department of Imaging Neuroscience, London, UK). The normalizing parameters were applied to the anatomical and ROI images, which were resampled to 2 mm of isotropic voxel size. Finally, all normalized anatomical images were averaged in order to have a brain template representative of our patient group allowing visualization of all ROIs. Left column: filled circles were plotted when at least one of the contact pairs exploring a given cerebral structure exhibited a CEPs response after PuM stimulation; empty circles: absence of CEP; yellow circle: CEP in patients with thalamic contact pair located in the posterior part of PuM (patients 1–4); blue circle: CEP in patients with thalamic contact pair located in the anterior part of PuM (patients 5–7). Right column: filled circles were drawn when stimulation through at least one of the contact pairs localized in a given cerebral structure evoked a PEP response; empty circles: absence of PEP; yellow circle: PEP in patients with thalamic contact pair located in the posterior part of PuM (patients 1–4); blue circle: PEP in patients with thalamic contact pair located in the anterior part of PuM (patients 5–7). CS, central sulcus; Sylv S, sylvian fissure; TOS, temporo-occipital fissure; Ins, insula; Fusif Gyr, fusiform gyrus.
responding to PuM stimulation (67%) was observed in the parahippocampal gyrus, whereas this rate was 47% in the temporal pole, 20% in the amygdala, and only 16% in the hippocampus. Unlike the temporal neocortex, mesial temporal structures also showed variable CEPs response rates among patients (see Table 2). Conversely, stimulation of these mesial temporal structures evoked very consistent PuM responses: parahippocampal gyrus and amygdala stimulation elicited PEPs in all patients, hippocampus stimulation in 4 of 5, and temporal pole stimulation in 3 of 6. Overall, a percentage of 80% of the stimulated contacts pairs located in mesial temporal structures were able to evoke PEPs (amygdala and parahippocampal gyrus: 100%; hippocampus: 83%; and temporal pole: 50%).

**Parietal--PuM Connections**

With a total of 34 contacts pairs (5 ± 4 per patient), the parietal lobe was the third more fully explored cortical area, after temporal neocortex and mesial temporal region. Functional connectivity strength varied greatly across parietal regions: The CEPs rate was 81% in the temporoparietal (TP) junction, with a small interindividual variability, whereas it dropped to 46% in the precuneus gyrus. In the postcentral gyrus, the only patient tested did not present CEPs. Thus the PuM-TP functional connectivity, including that of the angular and supramarginal gyrus, was comparable to that of the temporal neocortex regarding CEPs, whereas reciprocal connections looked slightly weaker with 67% of PEPs’ responses.

**Insula and Frontoparietal Operculum--PuM Connections**

With the superior temporal gyrus (see above), the insula and the frontoparietal operculum were the 2 structures showing the highest CEPs rate after PuM stimulation, with 94% and 85% of CEPs positive contacts pairs, respectively. CEPs were recorded in all patients with insular recordings. In all, 100% of the insular contacts pairs were CEPs positive in 5 patients and 67% in 1. Frontoparietal operculum CEPs rates were 100% in 3 patients and 50% in the fourth patient tested. However, unlike the temporal neocortex and the TP junction, the reciprocal corticothalamic functional connectivity was consistently much weaker. All together, only 14% of the stimulated contact pairs located in these 2 regions were able to elicit PEPs. No PEPs were recorded in response to stimulation of the frontoparietal operculum, in the only patient tested, and the PEPs’ rate after stimulation of the insula was only 17% (PEPs present in 1 patient, absent for the other 4 tested).

**Cingulate Gyrus--PuM Connections**

No CEPs were evoked by PuM stimulation in the anterior part of the cingulate gyrus and no PEPs were recorded after stimulation of this area in 2 patients, whereas reciprocal functional connections were observed in 2 other patients between PuM and posterior cingulate gyrus (67% CEPs and 100% PEPs).

**Fronto- and Occipito--PuM Connections**

Twenty-five contact pairs explored the frontal lobe in 3 patients. We observed a relatively weak but constant connectivity in all these patients: 40% to 50% of CEPs but no PEPs in the orbital gyri (2 patients), 40 to 67% of CEPs, and 33% of PEPs in the dorsolateral frontal cortex (3 patients).

In 4 of the 5 patients whose occipital lobes were tested, 43% of PuM stimulations produced CEPs, and PEPs following cortical stimulations were recorded in only 1 out of 4 patients (25%). All the occipital contacts pairs recording or inducing EPs were situated in the extrastriate cortex (see Table 2).

**Morphology, Latency, and Amplitude of the EPs**

No distinct morphological pattern of CEPs and PEPs could be distinguished throughout the explored structures. CEPs responses were frequently polyphasic, made of one or several waves. Other morphological types were monophasic, biphasic, and repetitive responses (repetition of the same potential, separated by a significant interval with return to the baseline). For PEPs, morphological types were simpler, generally mono or biphasic. Some examples of CEPs and PEPs waves are given in Figures 2 and 4.

Mean onset latencies of CEPs and PEPs are given for each structure in Table 2. Most of CEPs’ onset latencies (65%) were equal or inferior to 30 ms and strongly homogeneous across patients as indicated by relatively small SD values. The shortest
CEPs latencies were observed in the temporal neocortex, the TP junction, and the insula (onset latencies <20 ms). In contrast, PEPs latencies were generally longer and more variable, except for some mesial temporal structures and TP junction. The limited number of values obtained in each structure did not allow statistical analysis except for the temporal lobe where we could compare neocortical versus mesolimbic EPs characteristics. A Kruskal–Wallis test revealed significant differences between these 2 structures ($P < 0.0001$), and Dunn’s multiple comparison post tests showed that CEPs onset latencies were shorter in the neocortical ($13.9 \pm 5$ ms) than in the limbic component ($58.3 \pm 42.2$ ms; $P < 0.001$), whereas onset latencies of PEPs were not significantly different (neocortex: $51.8 \pm 37.5$ ms, limbic: $34.9 \pm 17.8$ ms). Within temporal neocortex, onset latencies were shorter for CEPs ($13.9 \pm 5$ ms) than for PEPs ($51.8 \pm 37.5$ ms; $P < 0.001$), whereas in the mesiolimbic cortex, CEPs' ($58.3 \pm 42.2$ ms) and PEPs' ($34.9 \pm 17.8$ ms) onset latencies were not different.

Both CEPs and PEPs amplitudes showed large variations not only between patients but also between contacts pairs exploring the same structure (see Figs 2 and 4).

**Impact of Epilepsy on CEPs and PEPs Responses**

Cortical or PuM stimulation procedure never produced paroxysmal events like epileptic spikes or ictal subclinical discharges. We were also unable to distinguish distinct morphological patterns of response between contact pairs located in or out the seizure onset zone. The influence of epilepsy on the functional efficiency of a given pathway could be quantitatively evaluated only on data obtained within the temporal lobe, where a sufficient number of epileptic derivations could be compared with “nonepileptic” ones.

The following parameters were considered: percentages of CEPs and PEPs responses, onset latencies, amplitudes, and responses duration (Fig. 5). In the nonepileptogenic temporal neocortex, 91% and 62% of contact pairs exhibited CEPs and PEPs, respectively. In contrast, only 50% of contacts pairs exploring the similar but epileptogenic neocortex give CEPs as well as PEPs. In the mesiotemporal structures, we observed a similar trend between nonepileptogenic (40% CEPs, 91% PEPs) and epileptogenic areas (27% CEPs, 67% PEPs). However, only CEPs rate in temporal neocortex was significantly lower in epileptogenic versus nonepileptogenic cortical structures (Fisher’s $t$ exact test; 2-sided $P < 0.0001$). Onset latencies as well as response duration tended to be longer in the epileptogenic cortex, except for CEPs duration in limbic structures, but none of these trends was statistically significant (Fig. 5). No CEPs or PEPs amplitude difference between epileptogenic and nonepileptogenic tissue was observed whatever the stimulation site (cortical or thalamic) or the cerebral structure (neocortex or mesiotemporal) considered (Fig. 5).

**Response Rate and Distribution of Cortical Connectivity According to Contact Pairs Localization within PuM**

Because the localization of contact pairs within the PuM differed between patients, we attempted to determine if there was some topical organization of cortical projections within the PuM. For this purpose, we individualized 2 groups of contacts: group 1 patients (1–4) had contact pairs located in the medial and posterior part of PuM, whereas group 2 patients (5–7) had contact pairs in anterior part of the PuM (see Fig. 1).

In spite of large overlap (see Fig. 3), the CEPs rate was significantly higher in the temporal neocortex for stimulation of the posteromedial PuM (group 1: 88%; group 2: 61.4%; Fisher’s exact test, 2-sided $P$ value = 0.011). Conversely, in the mesial temporal region, CEPs rate was higher for stimulation of

**Figure 5.** Diagrams showing response rates, mean ± SD latencies, amplitudes and response durations in epileptic and nonepileptic temporal neocortex (left column), and mesial temporal structures (right column). For response rates, 2-sided $P$ values were obtained after statistical analysis using the Fisher’s exact test. For latency, amplitude, and duration values, the Student’s $t$-test or the Mann–Whitney test was applied depending of the Gaussian or non-Gaussian distribution of these values. $P$ values inferior to 0.05 are considered as significant.
the anterior part of PuM (group 2: 47.6%; group 1: 16%; Fisher's exact test, 2-sided P value = 0.027). Finally, there was no significant difference in CEPs rates in the insula and frontoparietal operculum for stimulation of anterior or posterior PuM contact pairs. Because of small numbers, this analysis could not be performed on CEPs in other cortical regions and for PEPs data.

Discussion

This is the first study dedicated to the PuM functional connectivity and based on depth simulation and EP recordings in the human brain. We observed that this connectivity concerns large cortical territories, involving all cerebral lobes to some different degrees, and is coherent with most of the anatomical data available in monkeys. In humans, preferential and fastest pathways were found to interconnect the PuM with the temporal neocortex, the TP junction, and the insuloopercular region.

Previous animal studies have established the validity of our methodology for testing connectivity, with a demonstrated parallelism between electrophysiological recordings and anatomical findings (Tanibuchi 1992). In humans, this technique has remained rarely used because it can be applied only in epileptic patients whose presurgical evaluation necessitates intracerebral electrodes implantation. Furthermore, the spatial sampling is limited to brain areas suspected to be involved in seizures onset or propagation and thus varies from one patient to the other. However, such depth stimulations and recordings provide a unique opportunity to map in vivo the functional connectivity that may exist between given cerebral regions (Brazier 1964; Catenoix et al. 2005; Zumsteg, Lozano, and Wennberg 2006; Zumsteg, Lozano, Wieser, and Wennberg 2006).

However, some confounding factors or technical issues deserve attention when interpreting our data:

1) Even if our electrical stimulations never provoked any epileptic spike or discharge when applied in the epileptogenic zone, it cannot be ruled out that the epileptic condition of the patients could modify the evoked responses, by increasing or decreasing the neuronal excitability in the stimulated or recorded areas. To test this hypothesis, we have studied separately EPs recorded from "epileptogenic" and "nonepileptogenic" cerebral tissue in the temporal neocortex and mesial temporal structures. In both regions, our results suggested a decreased connectivity and/or excitability (decreased response rate, delayed latencies) in the epileptogenic zone, which was statistically significant for CEPs in the temporal neocortex of our patients with TLE. Thus, we may have underestimated, but not overestimated, the functional connection between PuM and its cortical targets. Another interesting point is the pathophysiological significance of this result. FDG-PET studies in temporal lobe epileptic patients have found hypometabolic cortical and subcortical areas, which could correspond to the neuronal network involved during ictal process (Chassoux et al. 2004). For the thalamus, which has been found hypometabolic in numerous PET studies (see Mauguieré 2004 for review, Joo et al. 2005; Hashiguchi et al. 2007), it has been postulated that anatomical neuronal loss in the epileptic focus is the causal factor explaining the decreased glucose metabolism (Dlugos et al. 1999). Our results support previous PET findings and indeed suggest that functional connections are reduced between PuM and its epileptogenic target areas in patients with TLE.

2) Even with stimulation applied between 2 adjacent contacts separated by 1.5 mm, one issue concerns the volume of cerebral tissue effectively excited by stimulation (sphere of 4 mm radius, see Materials and Methods). This point is particularly critical to decide whether the physiological effects of our thalamic stimuli were limited to PuM or may have involved the whole pulvinar structure and eventually adjacent thalamic nuclei. Recently, Zumsteg, Lozano, and Wennberg (2006) have shown that bipolar stimulations delivered either in anterior, dorsomedian, or centromedian thalamic nuclei evoke specific pattern of distributed cortical responses coherent with the anatomical connectivity specific to each of these nuclei. Similarly, we observed differences between the functional cortical connections of anterior and posterior PuM suggesting that the effects of stimulation remains focal inside the PuM nucleus and consistent with a topical organization of PuM connections with the temporal lobe. Because of large distance, the effects of posterior PuM stimuli are unlikely to have spread to neighbor thalamic nuclei. Moreover, the higher CEPs rate in the mesial temporal regions after stimulation of the anterior PuM is unlikely to reflect a diffusion to nearby central lateral and anterior pulvinar nuclei because these nuclei are not known to be connected with mesial temporal structures. Lastly, we never observed CEPs in the striate cortex as expected in case of stimulus diffusion to the inferior pulvinar, which is connected with the striate cortex (Rezak and Benevento 1979; Lysakowski et al. 1988; Romanski et al. 1997; Adams et al. 2000).

3) Another issue is that of the stimulus spread to thalamocortical fibers, which might take origin in neighbor thalamic nuclei and travel through PuM on their way to the cortex. The anatomical position of the PuM within the thalamus makes this possibility very unlikely. PuM is the most caudal thalamic nucleus and its posterior part is bordered medially by the lateral ventricle (see Duvernoy 1991); more rostrally, PuM is bounded laterally by the lateral pulvinar subdivision, ventrally by the brachium of the superior colliculus, and dorsally by the lateral posterior nucleus (see Morel's [2007] atlas). Due to this anatomical configuration, there is no clear evidence of fibers passing through the core of the PuM, especially in its most caudal extent, contrasting with the presence of fibers bundles in the inferior and lateral pulvinar subdivisions (Robinson and Cowie 1997).

The opinion that our thalamic stimulations are likely to have involved specifically the PuM nucleus are reinforced by the fact that our functional connectivity results are coherent with most of conclusions from hodologic studies in nonhuman primates (Muñson and Mesulam 1984; Baleydier and Mauguieré 1985, 1987; Aggleton et al. 1986; Insauti et al. 1987; Yeterian and Pandya 1988; Baleydier and Morel 1992; Romanski et al. 1997; Gutierrez et al. 2000). In monkeys, the cerebral cortex represents the major part of PuM-connected structures, apart from some subcortical inputs, mainly from the deep layers of the superior colliculus (Benevento and Fallon 1975), and our study shows that PuM has also a widespread cortical
connectivity in the human brain. These connections are
developed almost exclusively with associative cortical areas,
even if some studies have reported few labeled cells in PuM
resulting from injections in primary somatosensory or auditory
cortex (De Vito 1978; De La Mothe et al. 2006). Among visual
cortical areas, PuM connectivity concerns extrastriate cortex,
particularly V4 and inferotemporal cortex (Weller et al. 2002;
Adams et al. 2000; Yeterian and Pandya 1997). PuM connectiv-
ity with auditory and somatosensory associative areas like
parietal BA 7 and 5, superior temporal gyrus, and superior
temporal sulcus have also been extensively reported (Baleyrier
and Mauguiere 1977; Yeterian and Pandya 1985; Baleyrier and
Morel 1992; Cappe et al. 2007; Trojanowski and Jacobson 1975;
Mauguiere and Baleyrier 1978; Yeterian and Pandya 1989,
1991; Hacket et al. 1998; Gutierrez et al. 2000). Moreover, PuM
interconnects with higher order cortex and “paralimbic”
associations areas, including insular, temporopolar, prefrontal,
orbital, parahippocampal and cingulate cortex, as well as the
amygdala (Jones and Burton 1976; Price and Amaral 1981;
Mufson and Mesulam 1984; Insauti et al. 1987; Yeterian and
Pandya 1988; Barbos et al. 1991; Romanski et al. 1997). Finally,
PuM has connections with frontal eye field areas (Huerta et al.
1986; Romanski et al. 1997).

In humans, we found that PuM connectivity is particularly
developed with the associative cortices of temporal and
parietal lobes and, to a lesser degree, with those of occipital
and frontal lobes. Consistent with these data is the finding that
no CEPs to PuM stimulation and no PEPs to cortical stimulation
could be recorded within primary somatosensory and visual
cortex, even if this result is to be considered cautiously given
the few number of contact pairs tested in these areas. Furth-
more, we showed that, quantitatively, functional and
reciprocal connections between PuM and associative cortical
areas concerned mostly the temporal neocortex and the TP
junction, each one with CEPs response rate superior to 80%
and PEPs response rate among the highest as well.

Some of our results, however, are slightly diverging from
animal studies. This is the case for the reciprocal PuM-insula
connections mentioned in some early monkey studies (Mufson
and Mesulam 1984; Romanski et al. 1997) but later neglected in
review articles (Augustine 1996; Shelley and Trimble 2004).
Our results emphasize that connection in humans by showing an
insular CEPs response rate greater than that of the TP
junction and nearly equal to that of the superior temporal
 gyrus, 2 structures known to be tightly connected with PuM.
However, we observed limited reciprocal connection from
insula to PuM. PuM might thus play a substantial role as an
inputs source in the multimodal functionlity of the insula,
extending from somatosensory, pain, and visceral domains to
numerous cognitive functions (Augustine 1996; Ostrowsky
et al. 2002; Shelley and Trimble 2004; Mazzola et al. 2006),
but with a weak reciprocal influence of the insular cortex.

Large discrepancies between CEPs and PEPs rates were also
observed in the mesiotemporal structures, where the CEPs’
response rate was the lowest of all the cerebral structures that
we tested (34%), whereas the PEPs’ response rate was the
highest, close to 80%. The asymmetrical connectivity between
PuM and the above-cited structures could appear surprising.
Generally, the connections between the major sensory
thalamic relay nuclei and cortex are considered as “reciprocal”
(for review, see Steriade et al. 1997). However, some
topographical mismatches between corticothalamic and re-
ciprocal thalamocortical pathways are known in monkey
(Darian-Smith et al. 1999; Kultas-Ilinsky et al. 2003). Due to
the restricted volume of our stimulations, only a limited part of
cortical areas have been explored thus biasing the amount of
PEPs toward low values. However, this bias does not explain
the high PEPs rates observed in some cortical structures
(mesial temporal structures and posterior cingulate gyrus). Our
results could thus reflect a true quantitative imbalance in some
reciprocal PuM-cortical pathways.

No connectivity has ever been found between pulvinar and
hippocampus proper in nonhuman primates, whereas we have
obtained CEPs as well as PEPs in some of our patients, resulting
in 16% and 83% response rates, respectively. Aggleton et al.
(1986) described pulvinar afferents from the subiculum, and it
cannot be excluded that our hippocampal stimulation has
involved this very neighboring structure.

The last of our results that differs from anatomical data in
monkeys concerns the amygdala connectivity. Whereas a slight
projection to PuM originating from the central amygdaloid
nucleus has been mentioned by Price and Amaral (1981), the
existence of a reciprocal pathway connecting PuM with the
lateral amygdala is well established (Jones and Burton 1976;
Romanski et al. 1997). Conversely, we consistently recorded
PEPs after amygdala stimulation, whereas CEPs were registered
in only 1 out of 5 patients tested. To summarize, our results
confirm the well-known PuM connectivity with mesial tempo-
rnal structures. They also suggest that, in humans, cortical mesial
temporal areas are able to modulate strongly PuM activity,
whereas they receive much weaker functional afferents from
PuM.

Our functional connectivity data may help to better integrate
and emphasize the role of PuM in previous hypothesis about
the functional role of the pulvinar nucleus, which is mostly
supposed to play a key role in visual attention processing and
selectivity (Shipp 2003, 2004). Most of the afferent fibers to
PuM conveying driving inputs to this nucleus arise from
associative cortical regions. This is opposite to what is observed
for first-order thalamic relay nuclei that receive only modula-
tory inputs from the cortex, whereas their major driving inputs
come from ascending subthalamic pathways (Guillery and
Sherman 2002, Sherman and Guillery 2002). Moreover, in the
human thalamus, PuM is one of the most highly stained nucleus
with calbindin (see Münké et al. 2000; Table 2), a calcium-
binding protein, which is a marker of the matrix thalamic
network (Jones 1998, 2001, 2002). These thalamocortical
matrix cells are characterized by glutamatergic projections to
superficial cortical layers, showing a fuzzy topical distribution
that spreads beyond cortical areas providing reciprocal cortical
projections. Such an organization of connectivity between
PuM and cortex would allow the modulation of corticocortical
networks, some of them dominating the others when
reinforced by their indirect but parallel corticothalamocortical
counterpart (Shipp 2003). Because of its extensive connections
with multimodal associative cortical areas, PuM as a whole may
be a nodal point where numerous simultaneous perceptions
converge and compete. In addition, the well-developed
corticothalamic limbic pathways that modulate PuM activity
may influence attention selectivity according to the emotional
context.

Lastly, our results are encouraging for patients with
pharmacoresistant epileptic seizures arising from insula and
TP junction, in particular in the language dominant
hemisphere. These regions, due to their deep anatomical situation or their functional importance, are poorly accessible to surgical resection. PhM is involved in temporoparietal seizures development (Rosenberg et al. 2006) and is tightly connected with temporal lobe and insula. Chronic electrical stimulation might thus be used to control the epileptic activity in these cortical regions.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

Funding

French Ligue Against Epilepsy; supported by the Hospices Civils de Lyon.

Notes

We wish to thanks Dr Jean Isnard and Prof. Philippe Ryvlin for their help in interpreting SEEG data. Conflict of Interest: None declared.

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