Patients with extratemporal lobe epilepsy do not differ from healthy subjects with respect to subcortical volumes

B Gärtner, M Seeck, C M Michel, J Delavelle, F Lazeyras

Background: Evidence from previous volumetric magnetic resonance studies has revealed that patients with chronic temporal lobe epilepsy show atrophy of distinct subcortical nuclei, predominantly ipsilateral to the focus side. We were interested to find out if there is also selective subcortical atrophy in patients suffering from long-standing extratemporal lobe epilepsy.

Methods: Thirty-one patients in whom pre-surgical evaluation unambiguously localized an extratemporal focus were included in this study. Using high-resolution magnetic resonance imaging, the volumes of the caudate nuclei, putamen, pallidum, and thalamus were measured bilaterally in both hemispheres and compared with measurements obtained in 15 healthy volunteers.

Results: No significant difference in volumes was found between the two subject groups, or in any subgroup of extratemporal lobe epilepsy patients, nor was there any relation to clinical variables such as age of onset, overall seizure frequency, or disease duration. However, patients who had no or only rare generalised tonic–clonic seizures seemed to differ from the other patients and controls in that they had smaller putamen volumes bilaterally (p<0.001).

Conclusion: We concluded that extratemporal lobe epilepsy in general is not associated with diminished volumes in the studied subcortical structures, which contrasts with findings in temporal lobe epilepsy patients. Thus, both entities differ both cortically and subcortically. However, we found that small putamen volume was bilaterally associated with absent or rare generalised tonic–clonic seizures, implicating the putamen in the control of the most disabling seizure type, independent of the site of neocortical focus.
good compliance (n = 15). In one patient, no reliable information on GTCS was obtained. The volumetric data of 31 patients with lesional and non-lesional extratemporal lobe epilepsy (ETLE) was compared with 15 healthy volunteers. Measurements were obtained from pre-operative high resolution MRI scans. No significant difference in age was found between both groups (table 1). Among the ETLE patients, nine had left anterior (LA), six right anterior (RA), nine left posterior (LP), and seven right posterior (RP) focus. One patient had a history of simple partial status; however, his exclusion did not affect the results. “Anterior” and “posterior” referred to the rolandic and Sylvian fissures—that is, “anterior” referred to frontal epilepsy, “posterior” to parietal, occipital, and posterior temporal foci. Independent of the side, patients with anterior epilepsy reported a higher seizure frequency compared with posterior epilepsy (p = 0.07), in accordance with well established clinical observations. At the time of high resolution MR acquisition, all patients were on various drug treatments, without predominance of a particular drug in any of the subgroups. Seventeen patients had undergone surgery, with the following outcome: 11 were seizure-free, 4 experienced significant seizure reduction of 80%, 1 patient had modest (around 50%) post-operative seizure decrease, and 1 patient was left without worthwhile improvement. In 19 patients, the MRI revealed focal abnormalities (table 2).

Measurement of subcortical volumes

The measurements were carried out blinded to diagnosis. MRI images were acquired on a 1.5T Eclipse system (Marconi Medical Systems, Cleveland, OH, USA). A volumetric gradient echo acquisition (echo time 4.4 ms, repetition time 15 ms, flip angle 25°, slice thickness 1.1 mm, field of view 256 × 15 ms, matrix size 192 × 256) was used for image acquisition. The volumetry protocol used to measure the subcortical nuclei was as described elsewhere. The anterior and posterior limits of the caudate nucleus and putamen were determined in the horizontal plane, parallel to the hippocampal plane. These points were then transposed to the coronal plane and reconstructed perpendicularly to the hippocampal level, then both structures were manually traced from the anterior to the posterior limit. The posterior end of the caudate nuclei was defined as that part of the tail that remained superior to the ventricle. For the thalamus and pallidum, the superior and inferior limits were identified in coronal images, and then transposed to horizontal slices in which both structures were traced manually in each slice from the superior to the inferior limit. The volumes were obtained by integration using a program available on the clinical workstation (Marconi Medical Systems).

In our previous study, there was no evidence of major diffuse cortical processes in this age group as calculated by the whole brain volume in both patients and controls, and consequently, the statistical analysis of the normalised subcortical volumes (by whole brain volume) and the non-normalised volumes yielded the same results. Absence of significant diffuse cortical atrophy was verified by visual analysis, and thus, in the present study, analysis was based solely on the non-normalised volume data.

Statistics

For group comparisons between the ETLE and control groups, and for the ETLE subgroups, one way analysis of variance was performed. The presence of a significant difference was assumed if a p-value of <0.05 was obtained. The significance level was set at p < 0.01 for computing correlation analysis using the Pearson product moment correlation, or Spearman’s R coefficient if small subject numbers were compared.

RESULTS

Comparing the volumes of all subcortical nuclei between the ETLE patients and healthy controls yielded no group effect—that is, overall subcortical volumetry did not differentiate between the patient and healthy subject groups. A significant structure effect (F(1,132) = 471.64; p<0.0001) emerged that was attributed to the different sizes of the subcortical volumes and a significant side effect (F(1,44) = 17.62; p<0.0001)—that is, on average, the left sided volumes were smaller than the right sided subcortical volumes in all subjects. One way analysis of variance computations among the four subgroups with respect to localisation and comparing these with the controls again did not show a group effect, but the structure (F(3,132) = 497.33; p<0.0001) and side effect (F(1,41) = 13.87; p<0.0006) did.

The volumes of the caudate nucleus, putamen, pallidum, and thalamus were compared between patients who had no or rare GTCS, those who had more frequent GTCS, and controls. Significant main effects for structure and for side were found again, and a significant group effect also emerged (F(2,42) = 5.29; p<0.009), attributed to smaller volumes in patients with no or rare GTCS. There was also a significant structure group interaction, indicating that the group difference was more predominant for certain structures (F(6,126) = 2.82; p<0.0131). One way analysis of variance performed separately for each of the four structures revealed that only the putamen contributed to the structure group interaction (F(2,42) = 11.56; p<0.0001). Indeed, smaller putamen volumes were noted bilaterally in the patients with no or rare GTCS compared with controls (F(1,28) = 12.89; p<0.0012) and patients with more frequent GTCS (F(1,28) = 22.00; p<0.0001; fig 1). There was no difference in putamen volume between controls and patients with frequent GTCS (table 3).

There was no significant difference in age of seizure onset or epilepsy duration between both GTCS patient groups, but there was a difference in age at evaluation (F(1,40) = 6.64; p<0.0032). Patients with frequent GTCS were younger than patients with no or rare GTCS (mean (SD) age 19.4 (10.5) years v 31.9 (13.8) years). However, age as a covariate in a one way analysis of covariance design did not change the level of significance between the two patient groups.

<table>
<thead>
<tr>
<th>Table 1 Epilepsy groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Control group</td>
</tr>
<tr>
<td>ETLE (n = 31)</td>
</tr>
<tr>
<td>LA ETLE (n = 9)</td>
</tr>
<tr>
<td>RA ETLE (n = 6)</td>
</tr>
<tr>
<td>LP ETLE (n = 9)</td>
</tr>
<tr>
<td>RP ETLE (n = 7)</td>
</tr>
</tbody>
</table>

Mean (SD); *given as seizures/month, mean (SD) (median).

ETLE, extratemporal lobe epilepsy; LA, left anterior; RA, right anterior; LP, left posterior; RP, right posterior.
Table 2  Patient demographics

<table>
<thead>
<tr>
<th>No</th>
<th>Sex</th>
<th>Age</th>
<th>Group</th>
<th>Age of onset</th>
<th>EEG focus</th>
<th>Aetiology</th>
<th>Op</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>25</td>
<td>LA</td>
<td>2.5</td>
<td>L prefrontal</td>
<td>L dorsolateral frontal dysplasia</td>
<td>Yes</td>
<td>50%</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>18</td>
<td>LA</td>
<td>7</td>
<td>L frontal</td>
<td>L dorsolateral frontal dysplasia</td>
<td>Yes</td>
<td>80%</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>45</td>
<td>LA</td>
<td>20</td>
<td>L frontal parasagittal and L frontaltemporal</td>
<td>L fronto-orbital and circinate cavernoma</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>17</td>
<td>LA</td>
<td>6</td>
<td>L frontal parasagittal</td>
<td>L anterior circinate dysplasia</td>
<td>Yes</td>
<td>NIL</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>30</td>
<td>LA</td>
<td>21</td>
<td>L frontopolar</td>
<td>Discrete atrophy of the L superior and middle frontal gyrus</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>7.5</td>
<td>LA</td>
<td>1.5</td>
<td>L frontopolar</td>
<td>L pre-rolandic transmante dysplasia</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>15</td>
<td>LA</td>
<td>11</td>
<td>L frontocentral</td>
<td>Unclear, small L frontal white matter lesion</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>23</td>
<td>LA</td>
<td>14</td>
<td>L frontal</td>
<td>Polymicrogyria in the L inferior frontal gyrus</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>21</td>
<td>LA</td>
<td>11</td>
<td>L frontocentral</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>17</td>
<td>RA</td>
<td>8</td>
<td>R frontotemporal</td>
<td>R fronto-orbital cavernoma</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>50</td>
<td>RA</td>
<td>6</td>
<td>R frontotemporal</td>
<td>R frontal inferior heterotopia</td>
<td>Yes</td>
<td>80%</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>20</td>
<td>RA</td>
<td>11</td>
<td>R frontotemporal</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>16</td>
<td>RA</td>
<td>2.5</td>
<td>R frontocentral</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>4</td>
<td>RA</td>
<td>1</td>
<td>R frontal lateral</td>
<td>R fronto-basal gliosis</td>
<td>Yes</td>
<td>70%</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>57</td>
<td>RA</td>
<td>56</td>
<td>R frontopolar</td>
<td>R fronto-orbital cavernoma</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>41</td>
<td>LP</td>
<td>10</td>
<td>L temporo-occipital</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>17</td>
<td>F</td>
<td>18</td>
<td>LP</td>
<td>4</td>
<td>L temporo-parietal et frontoparietal</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>16</td>
<td>LP</td>
<td>8</td>
<td>L temporo-occipital</td>
<td>L temporo-occipital vascular lesion</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>12.5</td>
<td>LP</td>
<td>9</td>
<td>L parietotemporal</td>
<td>DNET in the L culmen</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>15</td>
<td>LP</td>
<td>14</td>
<td>L temporo-occipital</td>
<td>DNET in the L posterior inferior temporal gyrus</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>21</td>
<td>F</td>
<td>28</td>
<td>LP</td>
<td>11</td>
<td>L temporo-occipital</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>18</td>
<td>LP</td>
<td>12</td>
<td>L temporal</td>
<td>L temporal dysplasia</td>
<td>Unknown</td>
<td>No</td>
</tr>
<tr>
<td>23</td>
<td>M</td>
<td>36</td>
<td>LP</td>
<td>32</td>
<td>L accipital</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>24</td>
<td>F</td>
<td>21</td>
<td>LP</td>
<td>7</td>
<td>L temporo-parietal</td>
<td>L temporo-parietal transmante dysplasia</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>25</td>
<td>F</td>
<td>21</td>
<td>RP</td>
<td>10</td>
<td>R posterior temporal</td>
<td>Low grade glioma in the R posterior superior temporal gyrus</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>26</td>
<td>M</td>
<td>49</td>
<td>RP</td>
<td>10</td>
<td>R superior parietal</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>27</td>
<td>F</td>
<td>40</td>
<td>RP</td>
<td>17</td>
<td>R posterior temporal</td>
<td>Ganglioglioma in the R posterior middle temporal gyrus</td>
<td>Yes</td>
<td>70%</td>
</tr>
<tr>
<td>28</td>
<td>F</td>
<td>46</td>
<td>RP</td>
<td>9</td>
<td>R temporo-occipital</td>
<td>DNET in the R lateral temporo-occipital gyrus</td>
<td>Yes</td>
<td>SF</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>27</td>
<td>RP</td>
<td>8</td>
<td>R parietal</td>
<td>Unknown</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>30</td>
<td>M</td>
<td>16</td>
<td>RP</td>
<td>7</td>
<td>R parieto-occipital</td>
<td>R occipital polymicrogyria</td>
<td>No</td>
<td>–</td>
</tr>
<tr>
<td>31</td>
<td>F</td>
<td>9</td>
<td>RP</td>
<td>7 mo.</td>
<td>R posterior temporal</td>
<td>DNET in the R posterior superior temporal gyrus</td>
<td>Yes</td>
<td>SF</td>
</tr>
</tbody>
</table>

Age and age of onset in years, unless otherwise indicated.
% Value in outcome refers to the amount of post-operative seizure reduction.
LA, left anterior/frontal; RA, right anterior/frontal; LP, left posterior (posterior temporal, parietal, occipital); RP, right posterior (posterior temporal, parietal, occipital); mo., months; Op, operated; NI, no information; SF, seizure free.

(F1,127 = 13.88; p<0.0009). In addition, if only patients who had no GTCS (n = 9) were compared with those with very frequent GTCS (>3/year, n = 5), no age difference was found, but the difference in putamen size remained (F1,123 = 13.20; p<0.0034). Additionally, within these two patient groups, no correlation between putamen volumes and age, age of onset, or duration of epilepsy was noted.

Overall seizure frequency (that is, complex partial and secondary generalised seizures) was not associated with abnormal subcortical volumes, either for all patients as a whole or within the different focus subgroups, as determined by correlation analysis.

Comparing all patients with a left sided (LA, LP) or right sided (RA, RP) focus to the controls did not yield significant differences. The same was true when patients with an anterior focus (LA, RA) were compared with those with a posterior focus (LP, RP) or with controls. Moreover, no major differences between patients with an MRI identified lesion (n = 19) or negative MRI (n = 12) and controls were found. Patients with a dysmyeloblastic neuroepileptic tumour or with dysplastic lesion (as suggested by the MRI and/or a very active epileptogenic focus in the EEG and/or histopathology; n = 16) were analysed separately, but were not associated with a particular subcortical atrophy pattern.

**DISCUSSION**

MR based volumetric measurements of subcortical structures differentiate patients with temporal lobe epilepsy from healthy subjects, but do not differentiate between patients with extratemporal epilepsy. Thus, temporal and extratemporal epilepsy differ not only in the site of cortical dysfunction but also in subcortical volumetric parameters. It has been well established that both patient groups are different with respect to the probability of post-operative seizure control, which is higher overall for TLE patients. It is tempting to speculate whether the presence or absence of subcortical volume changes contributes to this clinical observation.

However, ETLE patients who have never experienced, or who have had only rare GTCS, appear to be different from healthy subjects or patients with frequent GTCS. They show significantly smaller left and right putamen volumes. A previous volumetric study in patients with left temporal epilepsy found bilateral changes in lenticular volumes, although in our earlier study, which also included patients with right temporal epilepsy, we noted that only the ipsilateral putamen volume was significantly smaller. However, in both studies, no relation between subcortical volumes and the frequency of GTCS was found. Again, this observation indicates that temporal and extratemporal epilepsy seem to differ in their profiles of subcortical atrophy.

It is not clear why putamen atrophy should occur in patients with no or rare GTCS. The finding of subcortical nuclear atrophy independent of epilepsy duration and seizure frequency indicates that selective subcortical atrophy is not a secondary finding of a longer or more severe epilepsy disorder, but rather present from disease onset. However, longitudinal studies are warranted to confirm this hypothesis. The putamen receives projections from the whole neocortex—that is, from temporal and extratemporal lobes. Most cortical areas project only to the ipsilateral putamen, but motor, pre-motor, and somatosensory regions are distributed bilaterally. Within the putamen, a somatotopic organisation has been described, with leg, arm, and facial
representation from dorsal to ventral. Other afferent fibres originate in the centromedian thalamic nucleus and the substantia nigra. Efferent fibres from the putamen project directly to the substantia nigra or, quantitatively more importantly, converge to the ventral pallidum, from where they project to the thalamus, substantia nigra, or subthalamicus. The information to cortical regions is processed via these structures, in particular from the thalamus to the motor and pre-motor cortex. Thus, the putamen assists in sensorimotor integration. It can therefore be speculated that the impairment of this integrative and modulating function, caused by a functional and/or anatomical anomaly in the putamen, promotes excitation overload, as in GTCS. A smaller putamen might then serve as a barrier against such information excess and consequently inhibit the modulating function, caused by a functional and/or anatomical anomaly in the putamen, promotes excitation overload, as in GTCS. A smaller putamen might then serve as a barrier against such information excess and consequently inhibit the progression from a complex partial to a generalised seizure. Any medical or surgical interference at the putamen level that leads to the abolition of this most disabling and dangerous seizure type will have a significant impact on patients’ care and should be subject to more detailed studies.

In our study, the age at evaluation was different between the GTCS groups; patients with no or rare GTCS were significantly older. Age is known to affect the size of the caudate and lenticular nuclei, at least when very old (>60 years) and young (<35 years) healthy subjects are compared. It is, however, difficult to rationalise why only the putamen but not the other structures under investigation were affected by age in our study group. In neither of our subject groups, both relatively young, did age correlate with the volumes of the putamen or any other subcortical nucleus. Moreover, age as a covariate in the variance analysis did not change the significance of our findings. When considering only those patients at the extremes of the GTCS spectrum—that is, those who had no GTCS and those who had GTCS more than once per year, the age difference disappeared, but the difference in putamen size persisted. Thus, we feel confident that the difference in putamen size is due to GTCS frequency and not to age in this rather young patient population. This finding is also in accordance with our previous observations in patients with temporal lobe epilepsy.13 It seems more likely that the age difference reflects a different referral pattern—that is, patients with relatively frequent GTCS may be referred earlier to a specialised centre than patients with no or rare GTCS.

Among patients with focal epilepsy syndromes, patients with extratemporal lobe epilepsy are often difficult to treat medically. Unfortunately they are often also difficult surgical candidates, especially if the MRI does not reveal distinct cortical anomalies. Vagal nerve stimulation appears to act on some of the subcortical structures, including the putamen,17 and this effect may explain its seizure attenuating effect in various epilepsy syndromes. Further studies on the subcortical network in patients with various chronic epilepsy syndromes, with and without GTCS, are needed to develop effective tailored treatment options.

ACKNOWLEDGEMENTS
This study was supported by the Swiss National Science Foundation (grant nos 3100–065232, 3100–052933, 31–067105.01/1, 3200–068105.02) and the Fondation Vaudoise Genève. We are grateful to S Zaim for helpful discussion of the manuscript.

Authors’ affiliations
B Gärner, M Seel, Laboratory of Presurgical Epilepsy Evaluation, “Functional Neurology and Neurosurgery” Program of the University Hospitals Lausanne and Geneva, Switzerland
C M Michel, Functional Brain Mapping Laboratory, University Hospital of Geneva, Switzerland
J Delavelle, F Lazeyras, Department of Radiology, University Hospital of Geneva, Switzerland

Competing interests: none declared

REFERENCES
Clinical Evidence—Call for contributors

Clinical Evidence is a regularly updated evidence-based journal available worldwide both as a paper version and on the internet. Clinical Evidence needs to recruit a number of new contributors. Contributors are health care professionals or epidemiologists with experience in evidence-based medicine and the ability to write in a concise and structured way.

Currently, we are interested in finding contributors with an interest in the following clinical areas:

- Altitude sickness
- Autism
- Basal cell carcinoma
- Breastfeeding
- Carbon monoxide poisoning
- Cervical cancer
- Cystic fibrosis
- Ecstasy use
- Grief/bereavement
- Halitosis
- Hodgkin lymphoma
- Hyperthyroidism
- Idiopathic thrombocytopenic purpura
- Inflammatory bowel disease
- Kawasaki disease
- Leukaemia
- Menorrhagia
- Meningococcal meningitis
- Meningitis
- Meningioma
- Meningiopathy
- Meningocele
- Malignant melanoma
- Malignant mesothelioma
- Melanoma
- Mental illness
- Mental retardation
- Mental retardation
- Meningeal carcinomatosis
- Multiple sclerosis
- Myasthenia gravis
- Myeloblastosis
- Myelodysplastic syndrome
- Myeloma
- Nasal cancer
- Necrotising soft tissue infections
- Neuroblastoma
- Neurofibromatosis
- Neuroleptic malignant syndrome
- Neurosarcoidosis
- Neuropathy
- Neurosurgery
- Nephrotic syndrome
- Nephraclisis
- Normal pressure hydrocephalus
- Osteogenesis imperfecta
- Otitis media
- Ovarian cancer
- Ovarian cyst
- Pancreatitis
- Paraneoplastic syndromes
- Patent ductus arteriosus
- Parkinsonism
- Pelvic inflammatory disease
- Peritoneal carcinomatosis
- Peritoneal mesothelial neoplasms
- Peritonitis
- Photodermatitis
- Primary biliary cirrhosis
- Primary biliary cirrhosis
- Primary liver cancer
- Primary pulmonary hypertension
- Primary sclerosing cholangitis
- Prostate cancer
- Prostatectomy
- Proteinuria
- Psoriasis
- Pulmonary embolism
- Rhabdomyolysis
- Rheumatoid arthritis
- Rheumatoid nodule
- Sarcoidosis
- Scleroderma
- Sickle cell disease
- Sjögren syndrome
- Small cell lung cancer
- Spermography
- Squint
- Systemic lupus erythematosus
- Testicular cancer
- Varicocele
- Viral meningitis
- Vitiligo

However, we are always looking for others, so do not let this list discourage you.

Being a contributor involves:

- Appraising the results of literature searches (performed by our Information Specialists) to identify high-quality evidence for inclusion in the journal.
- Writing to a highly structured template (about 2000–3000 words), using evidence from selected studies, within 6–8 weeks of receiving the literature search results.
- Working with Clinical Evidence Editors to ensure that the text meets rigorous epidemiological and style standards.
- Updating the text every eight months to incorporate new evidence.
- Expanding the topic to include new questions once every 12–18 months.

If you would like to become a contributor for Clinical Evidence or require more information about what this involves, please send your contact details and a copy of your CV, clearly stating the clinical area you are interested in, to Claire Folkes (cfolkes@bmjgroup.com).

Call for peer reviewers

Clinical Evidence also needs to recruit a number of new peer reviewers specifically with an interest in the clinical areas stated above, and also others related to general practice. Peer reviewers are health-care professionals or epidemiologists with experience in evidence-based medicine. As a peer reviewer you would be asked for your views on the clinical relevance, validity, and accessibility of specific topics within the journal, and their usefulness to the intended audience (international generalists and health care professionals, possibly with limited statistical knowledge). Topics are usually 2000–3000 words in length and we would ask you to review between 2–5 topics per year. The peer review process takes place throughout the year, and our turnaround time for each review is ideally 10–14 days.

If you are interested in becoming a peer reviewer for Clinical Evidence, please complete the peer review questionnaire at www.clinicalevidence.com or contact Claire Folkes (cfolkes@bmjgroup.com).