Potentials and EEG.

The patient was given clonazepam, valproic acid, and trimethadione with no relief of symptoms. Carbamazepine lessened the palatopharyngeal movement and also the muscle cramps in legs. Ear clicks and palatopharyngeal involuntary movements seen in our patient can be clinically classified into "palatal myoclonus," although the movements were not exactly rhythmic and occurred at a slower rate than the usual palatal movements. Needle EMG showed myokymic discharges in the palatal and mylohyoid muscles in synchrony with the movement. These EMG findings differ from those reported in "symptomatic palatal myoclonus" showing rhythmic discharges at a faster rate, although the previous EMG studies on "palatal myoclonus" did not disclose firing patterns in detail. Myokymic discharges and muscle cramps in the legs relieved by carbamazepine in the present case may indicate that they arise from neuromuscular hyperexcitability rather than a central motor disorder.

Ephaptic transmission resulting from demyelinization can cause focal myokymia, but in our patient there was no evidence of organic lesions in the posterior fossa, nor any other diseases suggesting diffuse injury or hyperirritability of the peripheral nerves, for example, in association with toxins, thyrotoxicosis, Guillain-Barré syndrome or polyneuropathy. Facial myokymia, though commonly seen in patients with pontine glioma, multiple sclerosis or Guillain-Barré syndrome, rarely involves the muscles innervated by lower cranial nerves.

Myokymic discharges, also called grouped fasciculations, usually cause vermicular movements, but involvement of the dorsal interosseous muscles may cause tremor-like or flickering movements of the fingers. Myokymic discharges in the palatal muscles could therefore cause movements resembling "palatal myoclonus" or "tremor." Needle EMG is important to differentiate palatopharyngeal myokymia from the essential "palatal myoclonus," which has a slower rate of movement than symptomatic "palatal myoclonus."

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**Buspirone in progressive myoclonic epilepsy**

Progressive myoclonic epilepsy is a clinical syndrome with obligate features of myoclonus and epilepsy and variable or inconstant features of dementia and ataxia. The most common is Unverricht-Lundborg disease (Baltic or Mediterranean myoclonus) but other types include Lafora disease and mitochondrial myopathy.

A serotonegic disturbance is suggested by reduced CSF-5 HIAA in Baltic myoclonus and the antimyoclonic effect of L-tryptophan plus a monoamine oxidase inhibitor or 5-hydroxy-L-tryptophan in some patients. The problem is that these observations do not point to a specific locus of abnormality in the 5-HT system.

Serotonin (5-HT) receptor pharmacology has advanced rapidly, identifying multiple 5-HT receptor types. Only a few have been studied experimentally in myoclonus. In rat, the full 5-HT$_1A$ receptor agonist 8-OH-DPAT induces myoclonus but partial 5-HT$_1A$ agonists such as buspirone do not.

This pilot study was intended as a preliminary step in the exploration of the possible role of 5-HT$_1A$ receptor abnormalities in progressive myoclonic epilepsy. The 5-HT$_1A$ receptor is key to the 5-HT containing raphe neurons on which it is located, because its stimulation decreases cell firing. The activity of these neurons may be especially important in brainstorm-mediated myoclonus, but the raphe nuclei also project widely to forebrain and spinal cord. Buspirone (Buspar) is the first clinically used 5-HT$_1A$ agonist of its class, widely prescribed as an anxiolytic. Since anxiety increases myoclonus in our patient population, we also hypothesised that they may benefit from an anxiolytic. Much evidence suggests buspirone exerts its clinical effect by stimulating pre-synaptic 5-HT$_1A$ receptors.

Two male and two female patients, aged 15–22 years, with progressive myoclonic epilepsy who had failed conventional therapy were identified. Standard diagnostic tests had been performed including muscle enzyme histochemistry. All were taking one or more anticonvulsants (valproic acid, clonazepam, lorazepam, or phenobarbital) for control of seizures, but none of the drug doses were changed during the study. Each patient had prominent action myoclonus, some spontane- nous myoclonus, and little or no cerebellar ataxia. None of the patients were seizure-free for more than a few months before the start of the study. All had therapeutic anticonvul- lusant levels before and during the study.

Patients were enrolled in an off label uncontrolled dose-ranging trial of buspirone using anxiolytic dose guidelines. The starting dose was 5 mg orally three times a day. The dose was increased every 3 days by 5 mg to a maximum of 60 mg/d. Two of the patients were videotaped performing a standardised battery of clinical tests including Archime- des’s spirals. Repetitive motor tests and myoclonus were scored using established scales. In patients who were neurologically impaired to comply with testing, a simple Likert scale was used to evaluate myoclonus: 0 = absent, ++ = moderate, +++ = severe.

Myoclonus was unchanged in one patient and worsened in three (table). Patient 1 left the study at the starting dose reporting it made her more unsteady and therefore she could not be tested. Patient 1, the only employed patient, could not go to work at 60 mg/day. On the Myoclonus Evaluation Scale, patient 1 went from 20% abnormality at baseline to 33% abnormality on buspirone; patient 2 from 43–56% to 47–53%, respectively. There were also no large differences on 10 timed motor tasks. Patient 4 was too impaired to comply with formal testing, but his action- and sensory-evoked myoclonus appeared to increase while spontaneous myoclonus was unchanged.

In all cases, the worsening of myoclonus was transient once the drug was stopped, and patients reported returning to their baseline level of function.

None of the patients experienced increased seizures compared with their baseline, even those with exacerbation of myoclonus. A brief head-shaking seizure occurred in patient 1 at 45 mg/day buspirone, a generalised convolution in patient 2 at 30 mg/day and in patient 4 at 20 mg/day. No new dyskinesias were evoked.

The incidence of irritability and sedation in our patients was higher than the 2% and 10% of 477 cases in the Physician’s Desk Reference, respectively. There may have been less difference when using 15 mg in the PDR.

This uncontrolled observational study in a small number of patients suggests that buspirone does not help and may exacerbate myoclonus in progressive myoclonic epilepsy. Worsening of myoclonus was not explained by decreased anticonvulsant levels, and there are no experimental data to support an interaction between buspirone and anticonvulsants. Although a fluctuating baseline of patients with progressive myoclonic epilepsy could give the false impression of drug-induced exacerbation, the patients improved when buspirone was discontin- ued.

The data should be viewed as positive findings for several reasons. Any response to buspirone suggests that the 5-HT$_1A$ somato- motor deterrent or effect is important, and by inference, that 5-HT-containing raphe neu-
rons are also present. It also implies that the 5-HT terminal is functional enough to medi- 
ediate decreased 5-HT tone. This interpretation is supported by the finding of reduced CSF 5- 
HT-AAA in some patients.

The second observation was that buspirone did not exacerbate seizures unrelated to 
myoclonus in progressive myoclonic epilepsy. Decreased excitation of myoclonus 
may precipitate myoclonus-associated seizures, perhaps as in our case 2. This supports the clinical observation that myoclo- 

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MATTERS ARISING

Balint’s syndrome in subacute HIV encephalitis

I was interested to read the report of Dr Schneider et al on a 45 year old woman with 
Balint’s syndrome complicating subacute HIV encephalitis.1 Attributing her cognitive 
disorder to subacute HIV encephalitis in the absence of biopsy confirmation is presum- 
tuous and likely to be incorrect. Focal neuro- 
ological findings are distinctly unusual with 
this disorder. It is far more likely that 
progressive multifocal leukoencephalopathy 
(PML) was responsible. PML affects approx- 
imately 4% of all AIDS patients.2 A predilec- 
tion for the parieto-occipital region is typical 
and visual disturbance a prominent man- 
festation in 35% of patients.3 The radi- 
ographic characteristics of the white matter 
lesions in PML4 mirror those observed in 
their patient. Furthermore, the improvement with zidovudine hardly dispels the diagnosis 
of PML. Spontaneous recovery5 and improvement following the use of zidovu- 
dine have both been reported with HIV- 
associated PML.

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Schneider et al reply:

We appreciate the comments by Dr Berger regarding the historical nature of the 
lesions in our patient who presented with 
Balint’s syndrome as the first neurological 
manifestation of AIDS.5 Unlike some 
patients with Balint’s syndrome due to stroke 
in whom visual movement perception is impaired,2 she perceived movement particu- 
larly well. We ascribed this variant to a 
subcortical lesion site, as shown by MRI, that 
spares cortico-ortocortical connections between 
primary visual cortex and visual association 
areas. Both subacute HIV encephalitis and 
progressive multifocal leukoencephalopathy 
(PML) primarily involve subcortical white 
matter and would explain the findings in 
our patient. The differential diagnosis was not 
elaborated in our article as it was not the 
primary objective. We favoured the former 
diagnosis because the MRI showed a 
bilateral, extended, confluent lesions on 
T2-weighted images appeared more typical of 
subacute encephalitis7 and because of the 
response to zidovudine treatment.5 In the 
absence of a biopsy or neurological 
revision of our patient’s lesions remains conjectural and 
we agree with Dr Berger that PML is a 
serious consideration in this patient.

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Anti-acetylcholine receptor antibody 
measurement in myasthenia gravis

In a recent study, Clarke et al reported a 
deficiency of anti-acetylcholine receptor (AChR) 
antibodies measurement in myas- 
thenia gravis (MG). In their retrospective 
study, antibodies were detected in only 38% 
of 86 patients with MG, compared with 
66–93% in other reports. The unusually low 
antibody detection rate is attributed by 
the authors to the use of pathological protein 
A for immunoprecipitation rather than anti- 
human IgG antisera. To support their 
claim, the authors cite our early report of 
36% detection in an assay employing protein- 
A. In that study, however, we observed 
rat muscle AChR as the antigen. Later, 
we modified the system using human ampu- 
tation muscle AChR protein which increased 
detec- 
tion to 88%, still insufficient to rule out the 
presciphating agent.2 These results agree 
with most reported series,6 which stress 
the notion that the assay efficiency (sensitivity 
and antibody titre) depends primarily on 
the quality of the antigen used. Thus 
protein-A is similar to anti-human IgG anti- 
sera for immunoprecipitation in the anti- 
AChR antibody assay and we feel that 
the authors should look for other method- 
ical flaws to account for the low sensitivity of their 
assay. Finally, we completely agree with 
the authors that all laboratories engaged in 
routine antibody assays should be subject to 
a quality control audit, and we wonder 
if the authors to consult with “EuroEQAS for 
AChR antibodies”.

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Buspirone in progressive myoclonus epilepsy.

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