

The internet

Don't slip through the net

R Al-Shahi, C Kennard

JNNP could help you become a technophile

It is possible to thrive in the modern world without recourse to the internet. But only just. If you are a “technophobe”, deterred by the daunting size and complexity of this continually evolving medium, *JNNP* could help you become a “technophile”.

Fewer than four decades ago, the cold war motivated the creation of the internet. Academic inspiration subsequently harnessed the internet's potential in its two best-known components: email and the world wide web. Born of a need for communication and maturing through a hunger for information, these two human desires have made the internet indispensable.

The overwhelming size of the internet makes it a formidable repository of knowledge. The figure below shows the Internet Software Consortium's latest internet domain survey (www.isc.org), which estimates that there are >160 million “hosts” and that their greatest proliferation has occurred in the last four years.

It is, of course, impossible to know how many people use the internet, but an educated guess is that ~580 million

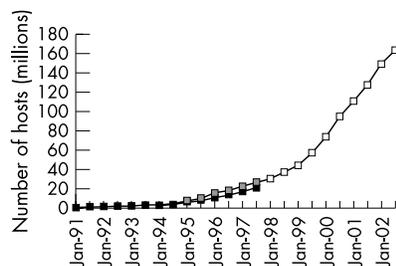


Figure 1 Internet domain survey host count. Reproduced with permission.

people across the world (almost 10% of the global population) were online in May 2002 (www.nua.com). Health is probably the largest single category of information hosted by the world wide web, and over two thirds of the online public—known as “cyberchondriacs”—seek information about it.¹

Despite its impact, the internet is still flawed. Access in the developing world remains limited, but initiatives like Digital Island seek to broaden the availability of material—such as *JNNP*—and make the world a smaller place.² While freedom to publish is part of the essence of the world wide web, cultural constraints will preclude consensus about what constitutes appropriate censorship.³ The notorious excess of poor quality information—largely due to lack of regulation and commercial exploitation—has become enough of a priority for the *BMJ* to devote its 9 March 2002 (*Evaluating the quality of health information on the internet*) theme issue to it. A recent survey is cause for some optimism; almost half of the “cyberchondriacs” in the USA and France were found to visit medical journals and academic or research institutions, closely followed by commercial health web sites.¹ Furthermore, the entire contents of two online evidence based health resources (*Clinical Evidence* and the Cochrane Library) were made available to the public in September 2002 through the National Electronic Library for Health (www.nelh.nhs.uk).

So how can *JNNP* help you cope with this immortal yet imperfect (but improving) medium?

Since 15 March 1999 the full text of the *Journal* has been available at

www.jnnp.com,⁴ as have customised @lerts, collected resources, and emailed tables of contents, with free back issues, rapid responses, and electronic manuscript submission via Bench>Press introduced recently. In this issue, the first of a series of review articles deals with the internet itself.⁵ Subsequent articles will focus on resources for neurology (including neurophysiology and neuroradiology), neurosurgery (including neuropathology), and psychiatry (including neuropsychiatry). Every review will be free at www.jnnp.com, and the recommended web sites are available as downloadable Bookmarks/Favorites at <http://jnnp.bmjournals.com/misc/bookmarks.shtml>. If you are already a “technophile”, or if we succeed in converting you, join us in our attempt to keep pace with the internet in the monthly *Neuroline* filler section.⁶

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Fetal striatal transplantation in Huntington's disease: time for a pause

R L Albin

The need to look at the rationale for fetal striatal transplantation

In this issue of the *Journal* (pp 678–685),¹ the NEST-UK consortium reports safety data on four subjects with Huntington's disease receiving unilateral intrastriatal transplantation of human fetal striatal tissue. This well designed and carefully executed study adds to the small amount of previous data on fetal striatal grafting for Huntington's disease.^{2,3,4} Groups in California and France reported a total of eight subjects receiving bilateral engraftment without complications and either no change in clinical outcome measures or some improvement.^{2,3} In another series of seven patients undergoing bilateral engraftment, there were four subdural haematomas (in three subjects), two requiring neurosurgical drainage.⁴ These latter subjects may have had more advanced Huntington's disease with a greater degree of brain atrophy, and this may be a contraindication to engraftment. The NEST-UK investigators plan a second phase safety study examining bilateral engraftment with a total of 10 subjects (including the four in the present report), and a two year follow up to generate preliminary efficacy data. This systematic approach is commendable.

The accumulated data, however, raise real questions about moving forward into efficacy trials. An incidence of two symptomatic subdural haematomas among 19

subjects is unacceptable. It is imperative that efficacy trials be controlled appropriately. The recent experience with fetal tissue engraftment for Parkinson disease revealed the existence of large magnitude and remarkably long duration placebo effects. Some form of sham surgery control is necessary. The NEST-UK protocol involves general anaesthesia, the surgery, a week of postoperative hospital care, and immunosuppression with frequent blood monitoring. Designing an adequate and safe sham surgery protocol will be a challenge.

The rationale for the fetal striatal transplantation is questionable. Successful striatal engraftment is likely to have limited effects. The hallmark of Huntington's disease is striatal degeneration, but the disorder affects the whole brain. There is significant whole brain atrophy, and neurodegeneration of the neocortex, hippocampal formation, thalamus, substantia nigra, and cerebellum have all been documented. Fetal striatal transplantation has shown efficacy in animal models of Huntington's disease, but these models use mainly toxin destruction of the striatum and do not mimic the systemic nature of Huntington's disease. If there were no alternative approaches, continued pursuit of engraftment would be rational. However, identification of the genetic defect in

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Huntington's disease—expanded CAG repeats within the *huntingtin* locus—resulted in an explosion of research on the pathogenesis of the disease. Recent advances include the development of several murine genetic models and the identification of various molecular processes as potential therapeutic targets. I believe the likelihood of an effective treatment emerging from these lines of investigation is considerably higher than the likelihood of marked improvement with fetal striatal engraftment.

Given the practical and theoretical objections to fetal striatal engraftment for Huntington's disease, the best approach would be for the NEST-UK investigators and other groups in this area to complete their safety trials and then pause.

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MRI scanning has become much more available over the last decade in many community hospitals, to the benefit of the populations they serve. There are some concerns, however, about quality control, and particularly because of the shortage of trained neuroradiologists. This important issue is addressed in the paper by Von Oertzen *et al* (this issue pp 643–647).²

It was found that MRI scans carried out and reported on in German community hospitals had a low rate of detection of focal lesions such as hippocampal sclerosis, tumours, cortical malformations, and vascular anomalies. There was a modest increase in detection rate by having these scans reviewed by expert neuroradiologists at the Bonn Epilepsy

Neuroimaging for epilepsy

Neuroimaging for epilepsy: quality and not just quantity is important

J S Duncan

Current resources for neuroimaging could be used more efficiently

The value of magnetic resonance imaging (MRI) of the brain in people developing epilepsy has been amply demonstrated.¹ This is particularly

the case for those with medically refractory partial seizures, for whom appropriate surgical treatment may result in complete resolution of seizures in 70%.

Centre. There was a greater increase in detection by obtaining epilepsy dedicated MRI in the centre, and focal lesions were identified in 85% of patients with unremarkable standard MRI.

Does this mean that all patients with refractory epilepsy need to be referred to specialist centres for their MRI scans? At present this would be an appropriate part of the evaluation for possible surgical treatment of the epilepsy, but it is also important to improve the diagnostic accuracy of MRI scans obtained at smaller units. There is some impact from improved scanning hardware, but the greater advance is possible from the use of MRI acquisition protocols for patients with epilepsy that may be used by radiographers without extensive specialist training. Protocols have been formulated in guidelines by the International League against Epilepsy^{3,4} that have also considered the complementary role of functional imaging with MRI.⁵ A typical basic epilepsy MRI protocol would comprise a T1 weighted volume acquisition which may be reformatted in any orientation

and used for volumetric measurements: proton density, T2 weighted, and fluid attenuated inversion recovery (FLAIR) acquisitions obtained with contiguous slices that cover the entire brain with as thin slices as possible and orientated perpendicular to the hippocampus. The oblique coronal orientation minimises partial volume effects that otherwise commonly obscure hippocampal sclerosis and small lesions in the temporal lobe, and also displays the rest of the brain in a clear and logical fashion. Standardisation of acquisition protocols also facilitates subsequent review of images at a specialist centre and may avert the need for repeat scans.

There is a clear need for an increased number of trained neuroradiologists to direct image acquisition and to report on MRI scans. In the meantime, current resources could be used more efficiently by the increased use of standardised acquisition protocols and effective tele-reporting in the managed clinical networks of community hospitals and regional specialist centres.

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Creutzfeldt-Jakob disease

CJD: are there distinct neuropsychological features?

R Knight

Different faces wearing the same expression: is there a core neuropsychological deficit in sporadic CJD?

As with many diseases originally defined on purely clinicopathological phenomenological grounds, “Creutzfeldt-Jakob disease” (CJD) has been subject to various “lumping” and “splitting” processes over the years.¹ The demonstration of laboratory transmissibility and the central role of the prion protein have served to unify the concept of CJD. Sporadic CJD (sCJD) remains, of course, defined by the absence of a known cause, in contradistinction to genetic, iatrogenic, and variant CJD. Despite this background unification, there is notable clinical phenotypic variation in sCJD including age of onset, duration of illness, and presenting symptom(s) in particular. Research has attempted to correlate these variations with molecular factors such as the *PRNP* genotype and the prion protein structure.² If sCJD is indeed a “spontaneous” disease due to a chance protein structural change or somatic *PRNP* mutation, then the different presentations

may simply reflect the usual function of the initially affected part of the CNS.¹ Whatever the explanation, the current view of sCJD is of an illness that may present in a variety of ways, including cerebellar ataxia, cortical blindness, dysphasia, and other deficits but which rapidly evolves into a global dementia with features of widespread brain disease. While attention has been given to the different modes of “physical” neurological presentation, there has been little comment on the pattern of cognitive dysfunction. A paper by Snowden *et al* (this issue pp 686–694) describes some detailed observations on five cases of sCJD (and one presumed familial case).³ The authors claim to have found a common, distinct neuropsychological profile despite different neurological presentations.

There are obvious reasons for the previous neglect of detailed cognitive assessments, as the authors indicate, including the rarity of sCJD and its rapid

clinical progression (mean duration: five months). Severe neurological impairment, even mutism, may be present at first neurological assessment.¹ It is therefore particularly notable that the authors were able to assess their cases, using neuropsychological tools previously developed for other dementias. Two particular findings, namely fluctuations in ability over time and variability of responsiveness will resonate with ordinary clinical observations of cases of sCJD and accord well with comments made by many relatives.

As the authors admit, these results are derived from only a small number of slightly atypical cases. One case was relatively young, four cases had longer than average durations and at least two were of unusual *PRNP* genotype. Further studies are therefore needed to confirm these preliminary findings.

Although sCJD shows us different faces, perhaps there is a single facial expression. Recognising this might be helpful in diagnosis, although other diagnostic techniques (such as the established csf 14–3–3 test and the developing role of cerebral magnetic resonance imaging) will be more useful.⁴ However, understanding this may help us to manage patients and better explain unusual phenomena to distressed relatives. Understanding may also help us to explore further the mechanisms of this terrible disease. Perhaps the most intriguing suggestions made by the authors relate to the possible anatomic and pathological implications of their findings.

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