ography shows hypometabolism in the orbital and prefrontal cortices). Paradoxically, levodopa and dopamine agonists (except selegiline at high doses, 30-40 mg/day) do not consistently alleviate depressive symptoms. In patients with fluctuating motor symptoms depression occurs when motor function is poor; more puzzling, deep brain stimulation, notably of subthalamic nuclei, can induce a delayed depression, although it improves motor function.[10]

Once depression is diagnosed, treatment is complicated by the drugs the patient is already taking. Due to the lack of systematic clinical trials there are still three main questions concerning the prescribing of an antidepressant.[3 4] The first is whether the antidepressant drug can increase or induce parkinsonian symptoms—tricyclic antidepressants such as desipramine, nortriptyline, and imipramine can improve motor symptoms, but selective serotonin reuptake inhibitors are repeatedly reported in case reports as potential inducers of parkinsonism. Fluoxetine is the only one to have been studied in this way, but a retrospective chart review by Caley and Friedman did not find that fluoxetine caused parkinsonian symptoms.[5] There are no data on the more recently launched antidepressants such as venlafaxine (a serotonin noradrenaline recapture inhibitor) and mirtazapine (a noradrenaline serotonin specific antidepressant).

The second question is the safety of antidepressant drugs in patients with Parkinson's disease. Tricyclic antidepressants can cause delusions, cognitive disorders (due to their anticholinergic effect), or orthostatic hypotension (they block adrenergic alpha receptors). The third question concerns interactions between antidepressant and antiparkinson drugs. Only one drug combination seems to be risky for patients: selective serotonin reuptake inhibitors (such as fluoxetine and fluvoxamine) and selegiline are associated with the potential and rare (the incidence is 0.24%) serotonin syndrome.[12] The diagnosis of serotonin syndrome is made on the basis of three of the following symptoms: a change in mental status (such as the onset of delusions, change in level of consciousness), myoclonus, sweating, hyperreflexia, tremor, diarrhoea, shivering, uncoordination, and fever. This syndrome can be fatal.

The depression associated with Parkinson's disease must be treated. The first choice is selective serotonin reuptake inhibitors (sertraline 50-200 mg/day; paroxetine 20-40 mg/day) or, in some countries and on an empirical basis, tianeptine (12.5 mg three times a day), which increases the presynaptic recapture of 5-hydroxy-indoleacetic acid, or moclobemide (300 mg/day), which is a reversible and selective inhibitor of monoamine-oxidase type. Adverse drug interactions are rare, except when selegiline is given at more than 5 mg twice daily. Clinical trials are needed not only to determine the risk-benefit ratio of these drug regimens but also to determine the optimum dose and duration of antidepressant therapy in Parkinson's disease.

Hervé Allain *head, department of experimental and clinical pharmacology*
Stéphane Schuck *assistant, unit of pharmacoepidemiology*
Nicolas Mauduit *research assistant, unit of pharmacovigilance*

University of Rennes I, 2 avenue Pr Leon Bernard, 35043 Rennes Cedex, France (Herve.Allain@univ-rennes1.fr)

Professor Allain has been given funding for clinical trials from Schering, Novartis, Roche, and Sanofi-Synthelabo. He has been paid for attending symposia by Schering, Janssen International, Pfizer Interntional, and Novartis.

1 Henderson R, Kurlan R, Kersun JM. Preliminary examination of the comorbidity of anxiety and depression in Parkinson's disease. *J Neuropsychiatry Clin Neurosci* 1992;4:257-64.
2 Menza MA, Robertson-Hoffman DE, Bonapace AS. Parkinson's disease and anxiety: comorbidity with depression. *Biol Psych* 1993;34:465-70.
3 Zesiewicz TA, Gold M, Chari G, Hauser RA. Current issues in depression in Parkinson's disease. *Am J Geriatr Psychiatry* 1999;7:110-8.
4 Cummings JL, Masterman DL. Depression in patients with Parkinson's disease. *Int J Geriatr Psychiatry* 1999;14:711-8.
5 Dooneef G, Mirabello E, Bell K, Marder K, Stern Y, Mayeux R. An estimate of the incidence of depression in idiopathic Parkinson's disease. *Arch Neurol* 1992;49:305-7.
6 Kostic VS, Filipovic SR, Lecic D, Mancilovic D, Sokic D, Sternic N. Effect of age at onset on frequency of depression in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1994;57:1265-7.
7 Taylor A, Saint-Cyr JA, Lang AE, Kenny FT. Parkinson's disease and depression: a critical re-evaluation. *Brain* 1986;109:279-92.
8 Mindham RH. Psychiatric symptoms in parkinsonism. *J Neurol Neurosurg Psychiatry* 1970;33:188-91.
9 Marder K, Tang MX, Cote L, Stern Y, Mayeuf R. The frequency and associated risk factors for dementia in patients with Parkinson's disease. *Arch Neurol* 1995;52:695-701.
10 Bejjami BP, Damie P, Anulf I, Thivard L, Bonnet AM, Dormont D. Transient acute depression induced by high frequency deep-brain stimulation. *N Engl J Med* 1999;340:1476-9.
11 Caley CF, Friedman JH. Does fluoxetine exacerbate Parkinson's disease? *J Clin Psychiatry* 1992;53:278-82.
12 Toyama SC, Iacono RP. Is it safe to combine a selective serotonin reuptake inhibitor with selegiline. *Ann Pharmacother* 1994;28:405-6.

The health hazards of mobile phones

The only established risk is of using one while driving

Despite repeated horror stories about mobile phones in the media, nearly half of the British public now owns one. Some 500 million people worldwide use mobile phones. Clearly, they have decided that the benefits outweigh any risks to their health. The benefits to the Exchequer in the United Kingdom are also substantial—£22bn ($13.75bn) from the recent round of bids for new licences. In this context, the publication of the *Report of the Independent Expert Group on Mobile Phones*, a group organised by the Department of Health, could have political implications.

Mobile phones are low power radio devices that transmit and receive radio frequency radiation (at frequencies in the microwave range of 900-1800 MHz) through an antenna used close to the user's head. Digital systems have recently replaced analogue. There is concern that microwaves might induce or promote cancer, and the symptoms associated with their use include sleep disturbance, memory problems, headaches, nausea, and dizziness.[1] Changes in the permeability of the blood-brain barrier, electroencephalographic activity, and blood pressure have

BMJ 2000;320:1288–9

also been reported.[2] The validity of many of these findings is uncertain, as are the mechanisms for such actions. Even so, rather than dismiss such concerns, the report says that there is sufficient anecdotal evidence to justify further research and taking a precautionary approach to the use of mobile phones.

UK guidelines are set by the National Radiological Protection Board and are based on the assumption that the only risk from microwave radiation arises from thermal effects—that is, from the heating of tissue that it can induce. Today's mobile phones, with a total power output of about 1 W, are estimated to produce insignificant local heating (equivalent to about a 0.1°C rise in temperature in the brain), which is unlikely to produce any deleterious effects. Although the recommended limits of exposure are similar in the United States and western Europe, there is no global consensus. Limits are stricter in some countries, especially Russia, where early research (albeit largely inadequately documented) led to concerns that microwave radiation too weak to cause serious amounts of heating might still pose risks to living systems.

Recent research from many countries suggests, however, that there are "non-thermal" effects on living tissue, ranging from immediate early gene expression and micronucleus formation to changes in the excitability of nerve cells, permeability of the blood-brain barrier, and the ability of rats to learn mazes.

Limits on exposure for workers have been suggested by the International Commission on Non-Ionizing Radiation Protection and are similar to those set by the National Radiological Protection Board. However, the commission recommended that the limit for the general public should be five times lower to provide additional protection for those who are ill or very young, since these groups may be more vulnerable. In the absence of stronger evidence that there is no risk from mobile phones, the recommendation of the independent group that these guidelines for public exposure should be adopted is prudent. So too are the report's recommendations to minimise power output and label phones with power ratings.

This is a controversial field of science. In vitro experiments on cell proliferation, membrane properties, and ion channels are difficult to extrapolate to humans. Moreover, it is also difficult to extrapolate effects on brain function and behaviour from rodents to humans because the entire brain of a rat or mouse is exposed but for a person using a mobile phone only the small region of the head that is close to the phone would be exposed. Although some studies have claimed to show an increase in DNA strand breaks in rats, others have failed to replicate this finding.[3–5] Concern was raised by the findings by Repacholi and colleagues of an increase in lymphomas occurring in transgenic mice that were prone to developing tumours and that had been exposed to microwave radiation for 18 months.[6] This work is now being repeated. The greatest mystery about non-thermal effects is their lack of a theoretical basis. Biological systems might interact resonantly with microwave fields but there is as yet no robust evidence.[7]

So far there is no clear evidence from epidemiological studies of a relation between mobile phone use and mortality or morbidity.[8] Tantalising findings in humans include a speeding up of reaction time during exposure, particularly during behavioural tasks calling for attention, and electroencephalographic changes during cognitive processes.[9–12] It is not clear, however, whether these findings have implications for health.

The only established health hazard cited by the independent group comes from the use of mobile phones while driving. The risk of an accident increases with age and is equivalent (when braking times are measured) to a blood alcohol level of 0.05%. The risk is the same when the phone is used "hands free" (via a loudspeaker), implying that it is due to the distraction caused by the conversation.

There are undeniable benefits in carrying mobile phones in vehicles: many lives have been saved by rapid reports of cardiac arrest and of serious trauma.[13] But the independent group's report is clear that even hands free mobile phones should not be used while driving.

Mobile phones have changed the way people work and communicate. But this independent group's report is right to recommend precautionary measures to encourage both manufacturers and users to limit microwave exposure until we can be more confident that the use of mobile phones is indubitably safe.

Michael Maier *senior lecturer*

Division of Neuroscience and Psychological Medicine, Imperial College School of Medicine, London W6 8RP
(Michael.Maier@ic.ac.uk)

Colin Blakemore *professor*

Laboratory of Physiology, University of Oxford, Oxford OX1 3PT
(blakemore@physiol.oxford.ac.uk)

Mika Koivisto *researcher*

Centre for Cognitive Neuroscience, University of Turku, 20014 Turku, Finland
(mika.koivisto@utu.fi)

Colin Blakemore is a member of the independent expert group on mobile phones. Mika Koivisto has worked on an independent research project examining the effects of mobile phones on brain function. This research was funded by Nokia, a manufacturer of mobile phones.

1 Hermann DM, Hossmann KA. Neurological effects of microwave exposure related to mobile communication. *J Neurol Sci* 1997;152:1-14.
2 Braune S, Wrocklage C, Raczek J, Gailus T, Lucking CH. Resting blood pressure increase during exposure to a radio-frequency electromagnetic field. *Lancet* 1998;351:1857-8.
3 Lai H, Singh NP. Single and double-stranded DNA breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation. *Int J Radiat Biol* 1996;69:513-21.
4 Chou CK, Guy AW, Kunz LL, Johnson RB, Crowley JJ, Krupp JH. Long term, low level microwave irradiation of rats. *Bioelectromagnetics* 1992;13:469-96.
5 Malyapa RS, Ahern EW, Straube WL, Mors EG, Pickard WF, Roti JL. Measurement of DNA damage by the alkaline comet assay in rat brain cells after in vivo exposure to 2450 MHz electromagnetic radiation. In: Proceedings of Second World Congress for Electricity and Magnetism in Biology and Medicine, Bologna, Italy, 1997.
6 Repacholi MH, Basten A, Gebski V, Noonan D, Finnie J, Harris AW. Lymphomas in Em-Pim1 transgenic mice exposed to pulsed 900-MHz electromagnetic fields. *Radiat Res* 1997;147:631-40.
7 Fröhlich H. The biological effects of microwaves and related questions. *Adv Electronics Electron Phys* 1980;53:85-152.
8 Rothman KJ, Loughlin JE, Funch DP, Dryer NA. Overall mortality of cellular telephone customers. *Epidemiology* 1996;7:303-5.
9 Preece AW, Iwi G, Davies-Smith A, Wesnes K, Butler S, Lim E, Varey A. Effect of a 915 MHz simulated mobile phone signal on cognitive function in man. *Int J Radiat Biol* 1999;75:447-56.
10 Koivisto M, Revonsuo A, Krause C, Haarala C, Sillanmaki L, Laine M, Hamalainen H. Effects of 902 MHz electromagnetic field emitted by cellular telephones on response times in humans. *Neuroreport* 2000;11:413-5.
11 Freude G, Ullsperger P, Eggert S, Ruppe I. Effects of microwaves emitted by cellular phones on human slow brain potentials. *Bioelectromagnetics* 1998;19:384-7.
12 Krause CM, Sillanmaki L, Koivisto M, Haggqvist A, Saarela C, Revonsuo A, et al. Effects of electromagnetic field emitted by cellular phones on the EEG during a memory task. *Neuroreport* 2000;11:761-4.
13 Chapman S, Schofield WN. Emergency use of cellular (mobile) telephones. *Lancet* 1998;351:650.