Correspondence

EDITED BY LOUISE HOWARD

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Crisis telephone consultation for deliberate self-harm patients

With reference to Evans et al (1999), it is not clear from the paper whether the ‘green card’ treatment group really received a different treatment from the control group. Did the control group receive advice concerning methods of accessing mental health services in the future (e.g. the general practitioner, crisis centre, ward, community psychiatric nurses, Samaritans)? This is particularly relevant as approximately 50% of each group were referred on to mental health services. This would have negated the effect of the green card as a valid different treatment intervention.

It would be helpful to know how many patients used the telephone support service after having been given the green card. It is possible that a poor telephone support service could have caused the apparent lack of positive outcome in the study. One wonders about the availability of on-call psychiatric trainees and their level of expertise in giving telephone counselling; additional information about this in the paper would have been appreciated.

The patients who had a history of repeated deliberate self-harm, probably represent a more vulnerable group, as stated in the paper, but they may also be a group who habitually use deliberate self-harm as a method of communication. Therefore, paying increased attention (in the form of the green card) to this dysfunctional behaviour may have exacerbated the behaviour.


M. Darelly The Hesketh Centre, 51–55 Albert Road, Southport PR9 0LT

Author’s reply: I wish to clarify some of the points raised by Dr Darelly. First, it is important to remember that both groups in our study received ‘treatment as usual’, while those subjects randomised to receive a green card also had the facility to access emergency telephone consultation. We know from our data that there were no significant differences between groups with respect to their management following deliberate self-harm (DSH) assessment, and it is important to remember that the management plan was presented to patients before randomisation to avoid any subsequent bias in the treatment offered. We did not document other advice given over and above the main management plan but this is likely in both groups to have included advice to consult with the patient’s general practitioner or psychiatric keyworker (if applicable).

Details of how the telephone support system was used, together with its effects on patients’ uptake of other routine medical and psychiatric services, are soon to be published in a separate paper (further details available upon request). Speculation about why the green card appears to have a detrimental effect in DSH patients with a previous history of self-harm and a positive effect in ‘first-timers’ must remain tentative as this was seen in the form of a large subgroup analyses. Further research, in the form of a large multicentre trial, is needed to clarify the effects of the green card on patients presenting with DSH for the first time.

The mechanisms for such effects of the green card are even more speculative at this stage. For first-timers (only a minority of whom will use the card) it is not clear whether knowledge that the care is there to be used should a crisis ensue (the ‘safety net’ hypothesis) is the most important ingredient or whether the consultation itself makes the difference. Further qualitative work in this area utilising patient interviews would be welcome. For some patients with a history of repeated DSH, it could be suggested that the green card may heighten their experience of gratification resulting from a use of self-harm as an albeit distorted form of communication. Another hypothesis might be that a brief, focused telephone consultation from a psychiatrist in training is not containing enough and actually increases self-harming behaviour in such individuals. It seems unlikely that this apparent paradox will be explored further in view of ethical considerations when proposing research methodology. However, it may well be a pertinent issue given the projected prominence of ‘NHS Direct’.

M. O. Evans Psychotherapy Department, Gaskell House, Swinton Grove, Manchester M13 0EU

Suicide attempts v. deliberate self-harm: a response

Ogunsipe (1999), citing Hawton et al (1997), states that deliberate self-harm is more common in females than males, although the difference is narrowing. In reply, Isometa & Lonnqvist (1999) write that Finland is the only country in Europe where males seem to have a slightly higher incidence of parasuicide than females. In Ireland, the National Suicide Research Foundation monitors hospital-treated parasuicide in one-quarter of the country. Forty-seven per cent of those treated are male and the male : female ratio is even closer to parity in urban areas. It is somewhat surprising to find that the Irish situation corresponds more closely to that in Finland as opposed to our British neighbours.

Both the Irish and Finnish data originate from centres of the WHO/EURO Multicentre Study of Parasuicide. The following standardised definition of parasuicide is utilised in all centres participating in this study. “An act with non-fatal outcome, in which an individual deliberately initiates a non-habitual behaviour that, without intervention from others, will cause self-harm, or deliberately ingests a substance in excess of the prescribed or generally recognised therapeutic dosage and which is aimed at realising changes which the subject desired via the actual or expected physical consequences” (Kerkhof et al., 1994). It is noteworthy that suicidal intent is not referred to in this definition. However, Isometa & Lonnqvist indicated that some degree of suicidal intent was required in their study. It is possible for Finnish males to have a slightly higher incidence of parasuicide, as defined by the WHO/EURO Study, and
for females to have higher rates when the presence of suicidal intent is required. If this were the case, it might help to explain how Isometa & Lonnqvist found a higher proportion of female suicides with previous suicide attempts.

Unfortunately, the issue of definition in suicidology continues to provoke controversy. The lack of standardisation limits our ability to make comparisons and generalisations based on the research findings of others, whether from the same jurisdiction or not.


M. Lawlor, P. Corcoran, D. Chambers
National Suicide Research Foundation, I Perrott Avenue, College Road, Cork, Ireland

Post-abortion mania
I was interested to read the report by Dr Mahe and his colleagues, describing a woman who suffered from five episodes of puerperal mania and two of post-abortion psychosis, one after a therapeutic abortion and one after a spontaneous abortion. This clinical observation is a valuable contribution to the literature.

The association of acute psychosis with abortion in women susceptible to puerperal psychosis has previously been noted in nine reports, starting with Esquirol in 1819. Some of the terminations were carried out in order to prevent a puerperal psychosis! This literature is summarised in my book Motherhood & Mental Health, pages 91–93. There is evidence, especially from Denmark (David, 1985), that abortion is a greater risk factor than a full-term pregnancy.


I. F. Brockington Division of Neuroscience, Department of Psychiatry, Queen Elizabeth Psychiatric Hospital, Mindelsohn Way, Birmingham B12 2QZ

Cognitive effects of antipsychotics in schizophrenia and relationship to quality of life
In his overview on cognitive effects of antipsychotics in schizophrenia Sharma (1999) stresses a relationship between cognitive function in schizophrenia and quality of life as an outcome measure. I think that Sharma’s use of the concept ‘quality of life’ has to be clarified to prevent a number of rather common biases. He quotes two studies that are said to support a relationship between cognitive function in schizophrenia and quality of life (Davidson & Keefe, 1995; Green, 1996). The term quality of life is not operationalised in the first study. In the second study, which is in fact an overview of other studies, it is reported by Heinrichs’ Quality of Life Scale (Heinrichs et al, 1984). Like most other instruments which have been used to detect the effect of atypical neuroleptics on quality of life in schizophrenia (Priebe et al, 1999) the Quality of Life Scale (subtitled “An instrument for rating the schizophrenia deficit syndrome”) assesses clinical judgements of negative symptoms of schizophrenia rather than subjective appraisals of quality of life made by the patient. As it seems reasonable to assume at least a moderate relationship of negative symptoms and cognitive functions in schizophrenia, it is not surprising that a relationship is found between cognitive functioning and quality of life when the quality of life measures seem to be confounded to a considerable extent by psychiatric symptomatology.

We think that it is necessary to make a distinction between quality of life as an evaluation criterion for illness-related phenomena (negative symptoms), and quality of life as a subjective assessment by the patient as a “subjective evaluation of oneself and one’s social and material world” (Orley et al, 1998) — that is, subjective quality of life, not as a disease but as a generic concept. Since there are some studies that show that cognitive functioning in schizophrenia may predict social outcome, and since objective social outcome is moderately (although surprisingly weakly) associated with generic subjective quality of life, some association between cognitive functioning and subjective quality of life is conceivable, but has not yet been supported by empirical evidence.

In a validation study of a German short form of the Lancashire Quality of Life Profile (Kaiser et al, 1999), equivalent to the English short form of the instrument MANSA (see Priebe et al, 1999), we did not find any significant correlation between any of the categories of the Wisconsin Card Sorting Test (WCST; Heaton et al, 1993) (number of categories, perseverative errors and responses, etc.) and the mean value of all satisfactions ratings, satisfaction with life as a whole and with satisfaction with mental health in a carefully selected sample of out-patients with DSM–III–R schizophrenia (American Psychiatric Association, 1987; n = 36; mean age—47 years; mean illness duration—19 years). Our conclusion so far is that whether or not subjective quality of life is related to cognitive deficits in schizophrenia (in attention or memory, besides deficits in executive functioning, which are seen on a variety of tasks, most notably the WCST) remains unclear and so far is only a hypothesis, although it is widespread as an advertising slogan for atypical antipsychotic medication.


with several years’ history of melancholic depression. At presentation she satisfied
full clinical criteria for non-psychotic major depressive disorder. Her medical his-
tory included ongoing problems with complex partial and generalised epileptic
seizures, seronegative arthritis, irritable bowel syndrome and migraine. A paternal
uncle suffered from schizophrenia but there was no other family history of psychiatric
illness. She had been a university student but discontinued her studies as a result of
her depression.

At presentation her daily medication included dothiepin 150 mg, carbamazepine
500 mg, lamotrigine 50 mg, mebeverine 405 mg, plus sumatriptan 50 mg and dihy-
drocodeine–paracetamol as required. Her antidepressant was changed from dothiepin
to the selective serotonin reuptake inhibitor (SSRI) paroxetine, increased to 30 mg daily,
and trazodone 30 mg at night. There fol-
lowed a dramatic and sustained improve-
ment in her mood and other depressive
symptoms.

In June 1997 she was diagnosed as having
essential thrombocythaemia with a platelet
count of 1400 x 10^9. Although distressed
by the diagnosis, no return of her depressive
symptoms was seen. Following unsuccessful
 treatment with dipyridamole, interferon
alpha was prescribed by her haematologist.
She was given 3 million units, stabilised at
three times weekly after her platelet count
fell to 700–800 x 10^9/l. She experienced
the usual flu-like symptoms, and after three
months noted the recurrence of depression
with a similar profile and severity as that
seen prior to treatment with paroxetine.

After six months of disabling depres-
sion, refractory to paroxetine plus in-
creased doses of trazodone and cognitive
therapy, she was admitted to hospital in
May 1998. She was reviewed by her haem-
atologist who discontinued interferon as
a result of the depression and started hydro-
xyurea 1000 mg daily. After two weeks this
was changed to anagrelide 500 µg twice
daily (prescribed on a named-patient basis)
together with atenolol 50 mg daily to re-
duce associated migraines. Her platelet
count was around 400 x 10^9/l. She had 11
bilateral electroconvulsive therapy (ECT)
treatments, administered twice weekly,
and had a good response. At the end of
 treatment she described her mood as being
90% back to normal. She continued on par-
oxetine 50 mg daily and trazodone 150 mg
at night and has remained psychiatrically
well to date.

Interferon alpha is associated with a
risk of depression, in some cases requiring
discontinuation of treatment (McDonald
et al, 1987). Treatment of interferon-induced
depression has yet to be evaluated by con-
trolled trials, but case reports have shown the
benefits of antidepressants (Goldman, 1994).

A notable feature of this case is that
interferon alpha appeared to reverse a pre-
existing antidepressant response to paroxe-
tine. This may be understood in terms of interferon’s capacity to impair serotonin
synthesis by inducing enzymes that de-
grade the serotonin precursor tryptophan
(Werner-Felmayer et al, 1989). Previous
research has demonstrated that dietary
tryptophan depletion can strikingly reverse
the antidepressant effect of SSRIs (Delgado

The clinical improvement seen in the pre-
cise case following hospitalisation may be
related to ECT, interferon discontinuation,
or both. Although discontinuation often gra-
dually relieves interferon-induced depression,
the rapidity and extent of response in the
present case suggests at least some effect of
the ECT. In contrast to the SSRIs, the anti-
depressant response to ECT appears resiliant
to tryptophan depletion (Cassidy et al, 1997).
We therefore suggest that ECT is more likely
than SSRIs to be effective in interferon-
induced major depression.

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R. H. McAllister-Williams, A. H. Young
Department of Psychiatry, University of Newcastle
up on Tyne, Leazes Wing, Royal Victoria Infirmary,
Newcastle upon Tyne NE1 4LP

D. B. Menkes Department of Psychological
Medicine, University of Otago, PO Box 913, Dunedin,
New Zealand.
Post-stroke depression

We read with great interest the paper by Gainotti et al (1999) and we wish to raise some concerns about their study.

Description of the statistical analysis was omitted from the paper and it is impossible for the reader to know how the data were analysed. The authors did not mention whether the patients were administered drugs usually given to stroke patients (e.g. steroids, beta-blockers and anticonvulsant drugs) and which can induce some depressive symptoms. In the section entitled “Criteria used to make a diagnosis of major depression”, the authors state that the validity of their diagnostic criterion (Hamilton Rating Scale for Depression (HAM–D) score > 17) has been documented by others (Salzman et al, 1994). This assertion is false – we find no scientific support in the Salzman et al paper for Gainotti et al’s assertion. Also, information on the clinical features of Gainotti et al’s sample is limited by their omission to report standard deviations and the mean age of patients with endogenous depression (see Table 1, p. 164).

The most important problem, however, is with regard to the interpretation of HAM–D scores across groups. It is not made clear whether the mean HAM–D scores reported in Table 1 are calculated across the whole sample or only within the group with depression. In the psychiatric literature a HAM–D score of < 12 is not generally considered clinically significant, so if Gainotti et al have calculated mean HAM–D score only within the group with depression, it is difficult to understand why the mean is so low (11.8 at < 2 months post-stroke). Alternatively, if mean HAM–D scores were calculated across the whole sample (i.e. patients with and without depression), the increase in the mean with increasing time post-stroke may be due simply to the increase in the relative number of people with depression (27% at < 2 and 2–4 months post-stroke, v. 40% at > 4 months post-stroke). In other words, the increase in the mean HAM–D score does not necessarily imply that the severity of depression in the whole sample increases from the acute to the later post-stroke period, but this tendency may be due simply to an increased proportion of patients with depression within the sample.

Finally, Cohen’s k for diagnostic concordance is not given by Gainotti et al. This index is routinely calculated when different diagnostic criteria are adopted for patient classification. Inspection of Table 1 shows that nine well subjects out of 43 were misclassified as having depression using the quantitative criterion of HAM–D score. This begs the question, how many patients with depression were classified as being well?


V. Di Michele State Department of Mental Health, via Berardinucci 95, 65123 Pescara, Italy
F. Bolino State Department of Mental Health, Sulmona, Italy

Authors’ reply: We would like to clarify some aspects of our paper in reply to the points highlighted by Di Michele & Bolino.

First, we would stress the fact that the preliminary analysis of our data had been extensive, but that only data relevant to the specific scope of our study, which consisted in checking the most recent version of Robinson and co-workers’ biological theory of post-stroke depression, were included in the manuscript. Our data are clearly inconsistent with this theory.

Regarding our data analysis, continuous data were treated using one-way analysis of variance, whereas frequencies of distribution were analysed by means of χ² tests.

The possible influence of drugs was checked in our study by excluding all patients who were taking at the time of examination (or had taken in the previous four weeks) antidepressant drugs. We did not check other drugs (such as steroids, beta-blockers or anticonvulsants) which could induce depressive symptoms, since they were not considered relevant for the specific scope of our study.

The patients with endogenous depression were matched as for age (60.1 years) and educational level (7.9) with the three groups of post-stroke patients. Only a slight difference in gender distribution was observed between stroke patients and those with endogenous depression (a preponderance of females (20:10) among the group with endogenous depression). This unexpected difference was not considered relevant with respect to the scope of the study.

Regarding interpretation of the HAM–D scores across groups, the main scope of our study consisted in determining whether the nature of post-stroke depression is different in the acute and in more chronic post-stroke periods. From this point of view, it was important to evaluate at various time intervals from stroke the qualitative aspects of depression and their anatomical–clinical correlates, whereas the severity of depression in patients with major depression was much less relevant. For this reason, the HAM–D scores were calculated, as the authors of the letter correctly argue, in each group as a whole (including subjects with and without depression) and the increment of the mean depression score across groups mainly reflected the relative increment of subjects with depression. Though this fact is not very relevant to the aim of our research, we must add that even considering only the patients with major post-stroke depression, we could observe a non-significant trend towards an increase in the mean HAM–D score from the acute (20.2) to the post-acute (21.8) and to the more chronic (23.5) post-stroke period.

Concerning the HAM–D score criterion for diagnosis of major depression and correlations between clinical and psychometric criteria, although different cut-off scores have been proposed in the literature, a score of 18 on the HAM–D is the most currently used (Endicott et al, 1981; Rapp et al, 1990). Furthermore, good concordance exists in our study between clinical (DSM–III–R) and psychometric (score > 17 on the HAM–D) criteria. We have measured this concordance on our data by the k statistic (Holman et al, 1982), which gives a numerical measure of chance-corrected categorical agreement. According to this index, which results from the ratio between the chance-corrected observed agreement and the chance-corrected perfect agreement, the perfect agreement corresponds to +1, the complete disagreement corresponds to −1 and the chance level is 0. The chance-corrected level of agreement between DSM–III–R criteria and HAM–D score > 17 was quite satisfactory in our study (k = 0.84).

Correlation between cerebral perfusion and depressive symptom scores from morning to evening

I am writing to point out an error in our paper on cerebral perfusion correlates of depressed mood (Ebmeyer et al., 1997). Although the description of methods in the paper is accurate, the interpretation of the interaction between condition (time of day) and depression scores (Befindlichkeitsskala (BFS)) is not accurate. This interaction does not represent the “within-subjects correlation with BFS change”, but the change in correlation between cerebral perfusion and symptom scores from morning to evening.

Consequently, “correlations with BFS” in the text ought to read “diurnal changes in correlations”. The reported “positive correlation between severity of depression and anterior limbic perfusion” is, in fact, a significantly stronger correlation between symptom scores and cerebral perfusion in the morning vs. evening. In other words, there is a relatively greater (positive) slope of the regression line between perfusion and symptoms in the morning, whereas the slope in the evening is significantly less positive. The correlations reported with factor scores were interpreted accurately and, for example, support the claim for a positive correlation between severity of depression/weakness/fatigue and anterior limbic perfusion.

Although this may seem an arcane point, the additional change in the ‘tightness’ of the mood-brain perfusion association from morning to evening implied by these results is actually rather exciting. It could reflect the difference between a direct and a compensatory relationship between brain activity and behaviour at different times of the day and should provide a motive for follow-up experiments.


K. P. Ebmeyer University of Edinburgh, Kennedy Tower, Royal Edinburgh Hospital, Morningside Park, Edinburgh EH10 5HF

Lithium-induced hypothyroidism

I would like to congratulate Johnston & Eagles (1999) on the scale of their study and for providing a clearer idea regarding the prevalence of hypothyroidism related to lithium and the potential risk factors. I would like to comment on several important issues, including the presence of pre-existing thyroid disease prior to initiation of lithium, the presence of antibodies and the possibility of diagnosis as a risk factor.

With regard to the presence of pre-existing hypothyroidism (as suggested by patients receiving replacement thyroxine) the study excluded a total of 18 cases, which, given the total number of cases on thyroxine, is a substantial proportion of the sample. This would suggest that patients who have hypothyroidism are more likely to suffer from conditions that require treatment with lithium.

It is unfortunate that thyroid antibodies were not measured more frequently. The finding that 13 out of 15 patients with hypothyroidism were positive for antibodies would suggest that the prevalence of antibodies would have been high and would have clarified the role played by autoimmunity in contributing to hypothyroidism. Thyroid autoimmunity mediating the hypothyroid effect of lithium has been studied extensively and there is considerable evidence to support this. As early as 1973, Crowe et al. (1973) suggested that two different types of hypothyroidism occur with lithium, one with evidence of underlying autoimmune hypothyroidism and one without, based on a review of cases reported. Studies by Lazarus et al. (1981) and Leroy et al. (1988) suggest a high prevalence for antithyroid antibodies in patients who are hypothyroid on lithium, thus supporting the role of autoimmunity mediating this effect. Indirect evidence that autoimmune factors may mediate the actions of lithium on the thyroid comes from cases of hyperthyroidism, a well-documented side-effect of lithium, that cannot be explained on the basis of a direct pharmacological effect of lithium on the thyroid.

The issue of a particular diagnosis being a potential risk factor for lithium-induced hypothyroidism has not been highlighted in the literature although it has been studied, albeit indirectly. It is reasonable to conclude from the literature that thyroid autoimmunity is increased in conditions in which lithium is likely to be prescribed (i.e. bipolar affective disorder and depressive disorders). A study by Lazarus et al. (1986), in which thyroid antibodies were investigated prior to the prescription of lithium, reported a prevalence of 43%. Importantly, the entire group had a diagnosis of bipolar affective disorder. This compares with only 8.6% in a study of unipolar depression (Joffe, 1987). This would indicate that there is a case for studying the relationship between the psychiatric diagnosis, thyroid autoimmunity and the hypothyroid effect of lithium. This could answer the question raised by the authors as to why hypothyroid patients on lithium are selected to remain on both treatments. It is possible that lithium is more likely to be continued when the diagnosis is that of bipolar affective disorder than depression alone.

I hope that further studies in this area will help to dissect out the factors that play a role in lithium-induced hypothyroidism.


S. Bhandari East Ham Memorial Hospital, Shrewsbury Road, London E7 8QR.
One hundred years ago

**Anti-alcoholic serum**

The Paris Academy of Medicine at its meeting of Dec. 26th listened to a very interesting paper communicated by MM. Broca, Sapelier, and Thiebaut on the discovery of a so-called anti-alcoholic serum which has already created a great deal of excitement in the daily papers and which looks rather like a trade advertisement. The three observers in question started from the principle that in alcoholic intoxication, as in morphia intoxication, there is a preliminary period which is characterised by gradual toleration of the drug and a feeling of desire for the poison. On the other hand, it is well known that certain organic poisons, more especially those produced by microbes, form in the organism antitoxins which represent the elements of resistance which the organism offers to infection. These antitoxins injected into another organism place that organism in a state of being able to resist the corresponding poison. The observers therefore determined to make research on these principles into the action of alcohol. They produced tolerance to alcohol in the horse by giving it by the mouth and then found that the serum of this horse inserted into other animals which had been made tolerant and fond of alcohol produced in the animals in question such a distaste to alcohol that they preferred to give up both eating and drinking rather than continue to take alcohol. The injection of this serum in large doses has produced neither in animals nor man any unpleasant symptoms either local or general. M. Broca and his colleagues proposed to call this substance “antiethyline”. Clinical experiments made upon drunkards had given most interesting and somewhat inconceivable results. The drunkard treated with antiethyline lost all his taste for alcohol; he no longer cared for brandy, rum, or absinthe, but he preserved a liking for wine and his appetite and strength returned. Up to the present antiethyline seems powerless to make any improvement in the organic alterations produced by the action of alcohol. It is only right to say that this thirsting serum which does away with any hungering after brandy but preserves the taste for wine was received by the Academy with smiling incredulity.

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Crisis telephone consultation for deliberate self-harm patients
M. Darely
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