Gedankenlautwerden will be experienced as painful and dangerous by the patient. *Selbstgespräch*, again in agreement with Dr Szasz, does describe a person who is talking to himself aloud. The author does not directly attribute the same meaning to *Gedankenlautwerden* as to *Selbstgespräch*, but in the way he introduces the two terms, one might (mis)understand the terms to be equivalent, which of course is not the case in German at all. As a matter of fact, we often may observe schizophrenic persons talking aloud to themselves, sometimes for hours. Describing this behaviour, we would use the word *Selbstgespräch*, even if we got the impression that the patient actually is answering arguments he experiences as coming from others. In his *Lehrbuch der Psychiatrie* Eugen Bleuler does not use the word *Sprachfehler*. He writes about speech in the context of accessory (not cardinal) characteristics of schizophrenia as follows:

'In speech, most schizophrenics don't show anything conspicuous. In our in-patients, however, disorders of this function are no rarity ... if the diseased do speak, the modulation of their voice may be non-normal, to loud, to low, to rapid, to slow, in falsetto, grumbling, grunting, staccato, precipitatedly, and so on. It happens, too, that some diseased don't open the mouth at all, whereby intelligibility will be reduced to zero, of course'.

May this letter contribute to lessen the treason of translation.

BLEULER, E. (1923) *Lehrbuch der Psychiatrie*, 4. Auflage, Springer, Berlin.

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SIR: Szasz believes that some symptoms of schizophrenia are 'Anglo-American inventions', mentioning as an example the English textbook of which Roth is a co-author. He blames this textbook's misinformation on a faulty translation of E. Bleuler's monograph on schizophrenia. He does not mention that the co-author, Mayer-Gross, of the same book, is a German psychiatrist who did not depend on a translation.

Instead of tracing some expressions like *Gedankenlautwerden*, which is of course a terminus technicus, to their sources and definition, he fiddles with some words or their literal meanings in dictionaries, and comes to the conclusion that *Gedankenlautwerden* and auditory hallucinations are the same. He also seems to think that schizophrenic speech disorder is something like stammering or a foreign accent, i.e. just an incoordination of muscles involved in speech.

Although Bleuler's term 'schizophrenia' has superseded the original 'dementia praecox', Bleuler's views on the illness were never generally accepted. However he describes at length what his patients told him about their symptoms, like hearing voices or hearing their thoughts, but are we to assume that Bleuler never realised that what they were telling him about their voices were similar to his own experiences. Had he not read Kant? Incredible! Plato? He obviously had forgotten! Otherwise he would have remembered that what patients described as their symptoms (like hallucinations) were just what he himself was having everytime he was thinking.

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Clozapine-induced hypersalivation and the alpha-2 adrenoceptor

SIR: In a letter to the *BJP*, Corrigan *et al* (1995) put forward the hypothesis that the troublesome side-effect of increased salivation seen in patients taking clozapine was due to the blockade of alpha-2 adrenoceptors by the drug. This proposal has some face validity since clozapine has considerable affinity for alpha-2 adrenoceptors (Richelson & Nelson, 1984), and alpha-2 adrenoceptor antagonists such as yohimbine increase salivation in humans.

Corrigan *et al* (1995) supported their hypothesis by referring to their observation, made in a single patient, that the alpha-2 adrenoceptor agonist lofexidine was effective in relieving clozapine-induced hypersalivation. This observation, together with an earlier report of the effectiveness of clonidine (Grabowski, 1992), another alpha-2 adrenoceptor agonist, would be consistent with an interaction between clozapine and the alpha-2 adrenoceptor agonists at alpha-2 adrenoceptors. However, since alpha-2 adrenoceptor agonists by themselves can reduce salivary output, the possibility cannot be excluded that the interaction between clozapine and the alpha-2 adrenoceptor agonists is at a physiological rather than at a pharmacological level. Indeed, it has been shown that muscarinic receptor antagonists, which reduce salivation by interacting with a different receptor system, are also effective in alleviating clozapine-induced hypersalivation (Fritze & Ellinger, 1995).

Thus the effectiveness of the alpha-2 adrenoceptor agonists fails to prove the hypothesis than clozapine-induced hypersalivation is due to alpha-2 adrenoceptor blockade.

Furthermore, there is evidence indicating that it is unlikely that the hypersalivation caused by clozapine is mediated by alpha-2 adrenoceptors. Firstly, the antidepressant drug mianserin which has a higher affinity for alpha-2 adrenoceptors that clozapine, not only fails to cause hypersalivation, but in fact it causes a significant (60% after a single dose of 20 mg) reduction in salivary output (Ogura *et al*, 1987). This effect of mianserin cannot be due to muscarinic receptor blockade since mianserin has a much lower affinity of muscarinic receptors than clozapine. Secondly, the atypical antipsychotic drug remoxipride also causes hypersalivation as a side-effect, however, it is a highly selective dopamine D_2receptor antagonist with extremely low affinities for other neurotransmitter receptors, including the alpha-2 adrenoceptor.

Thus, the way in which clozapine causes hypersalivation remains an enigma.

CORRIGAN, F. M., MACDONALD, S. & REYNOLDS, G. P. (1995) Clozapine-induced hypersalivation and the alpha-2 adrenoceptor. (Letter.) *British Journal of Psychiatry*, **167**, 412.

FRITZE, J. & ELLINGER, T. (1995) Pirenzepine for clozapine-induced hypersalivation. *Lancet*, **346**, 1034.

GRABOWSKI, J. (1992) Clonidine treatment of clozapine-induced hypersalivation. *Journal of Clinical Psychopharmacology*, **12**, 69–70.

OGURA, C., KISHIMOTO, A., MIZUKAWA, R., *et al* (1987) Comparative study of the effects of 9 antidepressants on several physiological parameters in healthy volunteers. *Neuropsychobiology*, **17**, 139–144.

RICHELSON, E. & NELSON, A. (1984) Antagonism by neuroleptics of neurotransmitter receptors of normal human brain in vitro. *European Journal of Pharmacology*, **103**, 197–204.

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Influences on cost effectiveness

SIR: Hotopf *et al*'s (1996) review of randomised controlled trials comparing the cost-effectiveness of SSRIs *v.* tricyclic antidepressants concluded that although SSRIs appeared to be safer and better tolerated, these advantages did not justify their extra costs. However, their review has not considered the fact that the cost of drugs is strongly influenced by regional economic factors such as the differing interpretations of drug patent rules, the production of generic drugs and the variable dose strengths of pharmaceutical preparations. To make this point clearer, I will elaborate from drug experience in India (using figures from *Drug Today*, January–March 1996). Altogether, there are 16 preparations of fluoxetine available with prices for 10 capsules of 20 mg strength ranging from 12 to 48 Rupees. If one excludes the single preparation costing 48 Rs, the mean cost for 10 capsules is around 20 Rs. Of note, none of the preparations are 'compound' i.e. combined with other psychotropic drugs. Two commonly used tricyclics in India are imipramine and amitryptiline. Both are commonly available in 25 mg and 75 mg dosage strengths; many preparations are compound with combinations usually being diazepam and chlordiazepoxide. For the sake of comparison, I only include pure pharmacological preparations of imipramine or amitryptiline. Taking the former, the mean cost of 75 mg preparations (strip of 10) is 13.9 Rs and for 25 mg preparations (strip of 10) is 5.1 Rs; equivalent prices for amitryptiline are 15.7 Rs and 7 Rs. Of note, the minimum price of 75 mg preparations for both tricyclics is 11 Rs.

It is important that any discussion on the cost-effectiveness of interventions (whether pharmacological or psychological) should stress that they are as much influenced by regional political and economic factors as by clinical outcome indicators.

HOTOPF, M., LEWIS, G. & NORMAND, C. (1996) Are SSRIs a cost-effective alternative to tricyclics? *British Journal of Psychiatry*, **168**, 404–409.

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Cytochromes and psychotropic drug interactions

SIR: Taylor & Lader (1996) have provided a timely editorial on the cytochrome P-450 enzyme system and the practical implications of its role in the metabolism of psychotropic drugs. It should not be overlooked, however, that the cytochrome P-450 enzyme system is also involved in the metabolism of commonly prescribed non-psychotropic drugs such as beta-blockers, type 1C antiarrhythmics and morphine derivatives, and knowledge of their pharmacokinetics is essential to avert adverse cytochrome-mediated drug interactions.

Although the authors rightly recommend the use of alternative drugs which interact to a lesser degree with the cytochrome P-450 system, they state