A.L., a 42-yr-old man has been in treatment at our outpatient clinic since 1992 suffering from psychotic manifestations following a second severe closed-head injury. The patient had his first contact with a psychiatrist 3 yr after his first severe head injury in 1962 (when 10 yr old). During his first hospitalization (in 1994) he presented with signs of affective flattening and behavioural problems and indications of borderline intellectual functioning or mild mental retardation. The patient underwent several surgical interventions. The early inter-operative period was complicated by behavioural problems and a lack of motivation. At that time his intellectual tests (WAIS) showed a decline of results to a level of 60–80 in verbal tests, with a significant decrease in performance results. However, after further surgery, his intellectual condition improved enabling him to complete a secondary-school education, get married and start work as an industrial worker. From that time onwards he had no contact with psychiatrists, nor did he receive any medication treatment.

In 1992 he suffered another severe closed-head injury, after a fall from a height of 9–10 m, with a resulting loss of consciousness for several weeks, requiring intermittent mechanical ventilation. Within a short time after this accident the patient started to hear voices that commanded him to injure himself or threatened him with impending death by a heart attack or stroke. The voices also gave a running commentary on all his actions, often giving ‘commands’ for trivial and obvious actions, such as ‘eat your meal’. Since 1992 the patient has been constantly psychotic, with hallucinations and delusions of a persecutory nature. Several treatments have been tried since 1992, but no improvement in his mental condition was achieved. His personality started to change and he manifested mood disturbances (mostly depressive) and rage outbursts directed toward his family. The patient was hospitalized 6 times during this period. The antipsychotic treatments he received during the past years have included doses of: haloperidol (up to 20 mg/d), thioridazine (up to 100 mg/d), perphenazine (up to 24 mg/d), clozapine (up to 120 mg/d), and penfluridol (20 mg/d). The antipsychotics were used as monotherapies or with antidepressants (e.g. fluvoxamine 200 mg/d) and mood stabilizers, such as carbamazepine (up to 1200 mg/d) or valproic acid (up to 1000 mg/d). The patient was subsequently noted to be abusing benzodiazepines. According to ICD-10 (World Health Organization, 1992) the patient’s diagnosis most closely resembles an organic hallucinosis. A CT scan performed in 1994, is shown in Figure 1. It should be noted that the patient’s compliance was inconsistent and his follow-up dates irregular. He made at least two violent suicide attempts. He was not able to return to work after 1992 and his family life was profoundly disrupted. In December 1997 olanzapine (Zyprexa) treatment was initiated at 10 mg/d, added to valproic acid (600 mg/d). Benzodiazepine treatment was gradually stopped. Some improvement in his mental condition was noted in subsequent follow-up. In February 1998 his dose was raised to 20 mg/d olanzapine with 600 mg/d valproic acid. Within 6 months of controlled therapy there was an obvious improvement in his mental condition.

![Figure 1](image.jpg) State after left frontal craniectomy, following head injury. Brain CT scan shows sign of left frontal gliosis with minimal ipsilateral shift of the frontal horn. Otherwise both ventricles, the midline and subarachnoid space components are normal (1994).
condition. The patient currently denies having imperative voices to injure or kill himself, which had terrified him for the past 6 yr. He does not have any delusional symptoms; however, he still has commenting voices. He is entirely compliant with his follow-up visits. His functioning and family relations have generally improved, he no longer has rage outbursts, his mood has improved and his behaviour is much more stable.

Olanzapine is a thienobenzodiazepine derivative which has been shown to be effective in patients with schizophrenia as well as related psychoses. It has structural and pharmacological properties resembling those of the atypical antipsychotic clozapine (Fulton and Goa, 1997). Binding studies show that olanzapine interacts with key receptors of interest in schizophrenia, having a nanomolar affinity for dopaminergic, serotonergic, α-adrenergic and muscarinic receptors (Bymaster et al., 1997; Moore et al., 1997; Nyberg et al., 1997). Electrophysiological studies indicate that olanzapine appears to have an atypical profile based on mesolimbic selectivity (Moore et al., 1997) and exhibits selectivity for mesolimbic (A10) pathways that mediate psychotic symptomatology. Although conventional antipsychotic drugs have been widely used to treat aggression, some authors believe that there is little evidence for their effectiveness in treating aggression beyond their sedative effect in agitated patients, or their antipsychotic effect among patients whose aggression is related to active psychosis (Buckley, 1990). Atypical antipsychotic agents (including olanzapine) may be more effective than conventional antipsychotic drugs in aggressive and violent populations, as they have shown efficacy in patients with dementia, brain injury, mental retardation and personality disorders (Buckley, 1990; Fava, 1997).

To our knowledge, this is the first reported attempt to treat a patient with an organic psychotic condition (organic hallucinosis) with olanzapine. We did not find any data about the use of olanzapine in organic psychotic states in an extensive Medline search. Despite the fact that the case presented here had an encouraging outcome, a single case cannot be taken as a definite indication of the efficacy of olanzapine in the treatment of organically based psychotic states. Additional reports of cases of novel antipsychotic drugs (including olanzapine) being used in organic psychotic states would provide important clinical data.

References
Buckley PF (1990). The role of typical and atypical antipsychotic medications in the management of agitation and aggression. *Journal of Clinical Psychiatry* 60 (Suppl. 10), 52–60.


Roberto Umansky and Vadim Geller
Beer Sheva Mental Health Center,
Faculty of Health Science,
Ben Gurion University of Negev,
PO Box 4600, Beer Sheva, Israel.