The presence of lupus anticoagulant and anticardiolipin antibodies in patients undergoing long-term neuroleptic treatment

Dear Sir:

Recently, we found low to moderate titres of anticardiolipin antibodies (aCL) in the serum of untreated patients with psychosis,[1] suggesting that aCL might play a role in the pathogenesis of psychosis. Elevated titres of aCL and lupus anticoagulant (LA) have been reported in patients treated with neuroleptics,[2] but have not been associated with clinical vascular events.[3] The objective of our present study was to analyze the prevalence of LA, aCL and their isotypes, among patients with psychosis undergoing long-term neuroleptic treatment.

Fifty patients with schizophrenia were included in the study (33 male, 17 female). The mean age of the patients was 43.4 years (ranging between 23 and 65 years). Patients fulfilled the diagnostic criteria of schizophrenia or schizophreniform disorder according to the *Diagnostic and Statistical Manual of Mental Disorders, 3rd edition, revised* (DSM-III-R). All patients were continuously treated over the past 5 years with at least 1 neuroleptic drug (phenothiazines and/ or butyrophenones); there had been no change in the neuroleptic administered during the 3 months preceding the study. None of the patients had any clinical or serological evidence of autoimmune disorders, history of epilepsy, abortions, vascular events, recent infection, or had been taking any medications other than antipsychotic drugs. Twenty healthy, age-matched donors, without a history of psychiatric illness, vascular events, fetal loss, or long-term use of medication, served as a control group.

LA was estimated by diluted Russell viper venom time and tissue thromboplastin inhibition test.[4] A commercial enzyme immunoassay kit (Cambridge Life Sciences PLC, UK) was used to measure aCL antibodies, and results were expressed according to the recommendations of the Second Workshop on Standardization and Interpretation of the aCL test.[5] Antinuclear antibodies were detected by an indirect immunofluorescence technique. The results were analyzed using the χ^2 test.

In 26 patients (52%), we detected either antiphospholipid antibodies or LA in serum. Of these 26 patients, 22 (44%) were positive for LA; 12 of these patients (24%) had raised titres of IgM-aCL, and 5 of these patients (10%) had raised titers of IgG-aCL (Fig. 1). In 10 patients we detected LA alone, in 2 patients we detected IgM-aCL alone, and in 1 patient we detected IgG-aCL alone. These results were significantly different from controls ($p < 0.0003$). All of the controls were negative for both aCL and LA. Tests for antinuclear antibodies had negative results in both the patients and controls.

The mechanism of neuroleptic-

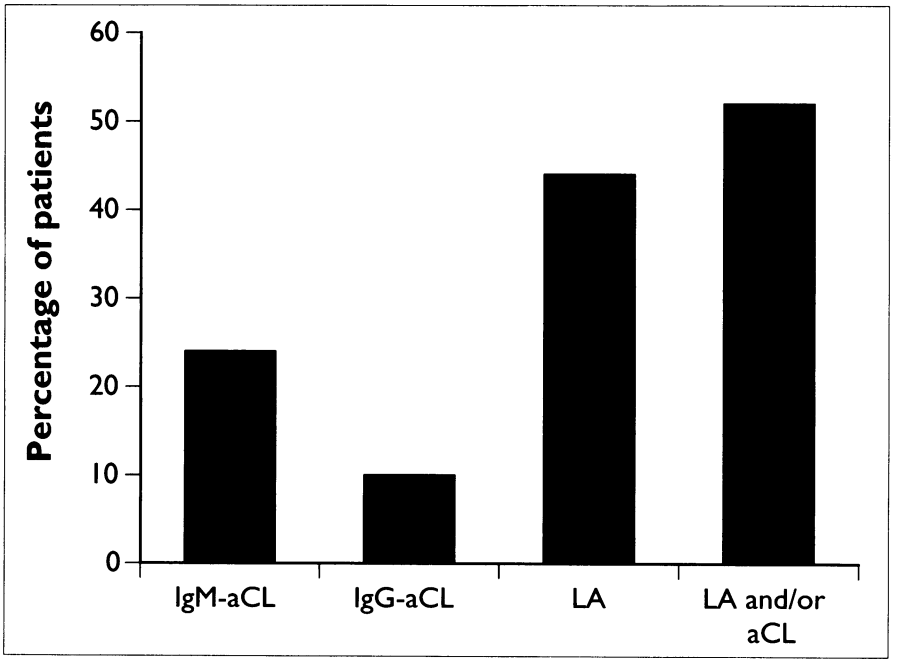

Fig. 1: Frequency of anticardiolipin antibodies (aCL) and lupus anticoagulant (LA) in 50 patients with schizophrenia undergoing long-term treatment with neuroleptics.

induced aCL remains unclear. The induction of aCL requires β-2-glycoprotein-1 as a cofactor for binding to cardiolipin.[6] It is assumed that neuroleptics can increase phospholipid expression and activation on the cell membrane, inducing aCL binding to cardiolipin epitopes without involving β2-glycoprotein-1. This causes the induction of mainly IgM-aCL rather than IgG-aCL (IgG-aCL is the main isotype related to thrombosis). This might explain the lack of vascular events in these patients.

We earlier reported the presence of LA activity and IgG-aCL in a group of patients with psychosis who were not taking medication and had no clinical evidence of vasculopathy.[1] These findings, together with our present study, raise the possibility that these autoantibodies are implicated in the etiology or course of psychosis. Sirota et al[7] reported the presence of different types of autoantibodies, including aCL, in patients with schizophrenia and their healthy first-degree relatives. Firer et al[8] found aCL antibodies in both patients with schizophrenia and their relatives. Roy Chengappa et al[9] propose that raised titres of IgG-aCL may be a marker for autoimmune reactivity or may play a role in schizophrenia. To support such a possibility, both the patients and controls were tested for the presence of antinuclear antibodies. The negative result in both groups does not support this notion; however, it can not be excluded, since the sample was relatively small.

This study re-established the association between long-term treatment with neuroleptic medication and LA and elevated aCL. Further studies are needed to clarify the role of antiphospholipid antibodies in these patients.

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Understanding autism: does anyone read new medical journals?

Dear Sir:

I read Dr. Peter E. Tanguay's editorial[1] with mounting interest after he started by citing Barr's 1898 case of autism,[2] since this is my first indication that anyone has read my 1982 letter drawing attention to this case.[3] Tanguay stated, "In this issue of the Journal (see page 103), Drs. Trottier, Srivastava and Walker present a remarkable review of this current literature. Their report is lively, well organized and very comprehensive." However, I was disappointed to find that this review article, with 124 references, made no mention of possible peripheral auditory defects or ear disease in autism, despite noting the relevance of sensory pathway integrity and devoting a column to auditory impairment.

For a quarter of a century I have been proposing that autism is an unusual variant of peripheral deafness.[3-24] Surely it is time that someone somewhere took this theory seriously and discussed it. If false, it should be trashed, if only to stop further valuable journal space being devoted to a nonviable theory. It is simple to the point of naïveté, so it should be easily refutable if it is incorrect. For example, all that is needed is to find some risk maker or risk marker for autism that is not also associated with middle- or inner-ear deafness.[17] I have looked quite hard and still not found one,