on the main outcome measures, as we reported in the original paper, nor did the antioxidant supplementation modify the effect of serum total cholesterol on suicide.

Tanskanen *et al* (above) report in their letter that the risk of suicide was increased with higher serum total cholesterol levels in random samples of Finnish smokers. We do not have any obvious explanation for these conflicting findings, but study populations were rather dissimilar. Their subjects (aged 25–64 years) were mainly from eastern Finland, whereas our subjects (aged 50–69 years) were from south-western Finland. The results of other cohort studies investigating the association of serum total cholesterol levels with death from suicide have been inconsistent, since there has been no association or the association has been inverse in previous studies. Tanskanen *et al*, as well as Su *et al* (above), raise the possibility of dietary fatty acids affecting the occurrence of depressive disorder, which in turn is one of the strongest risk factors for suicide. Our aim is to analyse, in subsequent studies, the relationships between various dietary factors (fats, carbohydrates, and amino acids), depressed mood and suicide risk.

**ATBC Cancer Prevention Study Group (1994)** The alpha-tocopherol, beta-carotene lung cancer prevention study: design, methods, participant characteristics, and compliance. *Annals of Epidemiology*, **4**, 1–10.

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## Motor responses to transcranial magnetic stimulation in schizophrenia

We read with interest the paper by Boroojerdi *et al* (1999). Our group found a shorter latency for motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) in unmedicated people with schizophrenia of, on average, 2 ms compared with age- and gender-matched normal subjects (Puri *et al*, 1996). In contrast, Boroojerdi *et al* (1999) reported no such latency difference (in their group of medicated patients) and speculated that the presence of antipsychotic medication may have confounded their results. Indeed, our group has previously reported the effects of such medication on the latency and form of the inhibitory silent periods to TMS (Davey *et al*, 1997), which is known to occur as a result of activating superficial intracortical inhibitory interneurons, possibly GABAergic (Davey *et al*, 1994). Boroojerdi *et al* (1999) found a longer latency of transcallosal inhibition to TMS in a group of medicated patients with schizophrenia but did not include a group of drug-naïve patients. It is clearly important to be able to differentiate between pathophysiological mechanisms resulting from schizophrenia and the actions of antipsychotic medication on the corticospinal system.

**Boroojerdi, B., Töpper, R., Foltys, H., *et al* (1999)** Transcallosal inhibition and motor conduction studies in patients with schizophrenia using transcranial magnetic stimulation. *British Journal of Psychiatry*, **175**, 375–379.

**Davey, N. J., Romaiguère, P., Maskill, D. W., *et al* (1994)** Suppression of voluntary motor activity revealed using transcranial magnetic stimulation of the motor cortex in man. *Journal of Physiology*, **477**, 223–235.

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**Puri, B. K., Davey, N. J., Ellaway, P. H., *et al* (1996)** An investigation of motor function in schizophrenia using transcranial magnetic stimulation of the motor cortex. *British Journal of Psychiatry*, **169**, 690–695.

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## Clozapine-induced thrombocytosis

Clozapine is known to cause blood dyscrasias, typically neutropenia and agranulocytosis. A raised platelet count, with clozapine as the sole implicated agent, had been reported to the Committee on Safety of Medicines in three cases. This is the first to be published.

A middle-aged male with ICD schizophrenia failed to respond to neuroleptic medication (haloperidol 25 mg/day, chlorpromazine 500 mg/day), or olanzapine at a dose of 20 mg/day for six weeks. He was therefore started on clozapine. He continued to receive droperidol 20 mg/day and zopiclone 7.5 mg nocte.

Fifteen days after commencing clozapine he complained of nausea. His clozapine was increased the next day by 25 mg to 300 mg/day. He complained of arthralgia and became hypotensive (b.p. 90/60 mmHg). Clozapine was stopped and the symptoms subsided over 36 hours. Clozapine was then restarted at a dose of 100 mg twice daily. He re-developed hypotension, arthralgia, malaise and sweating after one dose. He was apyrexial. Five days after the onset of nausea, the platelet count was $454 \times 10^9$/l (normal range: 150–$450 \times 10^9$/l), the erythrocyte sedimentation rate (ESR) 70 mm/h and the C-reactive protein 103. Eight days later the ESR had fallen to $<5$ mm/h but the platelet count had risen to $774 \times 10^9$/l. Five days later the platelet count had fallen to $393 \times 10^9$/l and subsequently returned to normal.

Muller *et al* (1991) reported fever 7–15 days after commencing clozapine in 12 patients with non-specific inflammatory parameters, including a raised white cell count, ESR and C-reactive protein. They did not comment on platelet changes. This case has similar symptoms but without pyrexia. The rapid re-emergence of symptoms on rechallenge suggests an immune response to the drug, and both thrombocytosis and thrombocytopenia are recognised features of such a reaction.

**Muller, H., Manns, M., Hammes, E., *et al* (1991)** Studies on inflammatory side effects of clozapine. *Biological Psychiatry*, **29** (suppl.) 415S–416S.

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## Paternal age and schizophrenia in dizygotic twins

Crow (1999) reported that dizygotic twinning increases with parental age as does the incidence of schizophrenia. Our study of 574 patients with schizophrenia showed that the incidence of schizophrenia increases with paternal age (Raschka, 1998). Scientific publications reported increased incidence of at least 12 illnesses with increased paternal age. The rate of mutations in spermatogenesis increases with age (Penrose, 1955; Vogel & Motulsky, 1979; Raschka, 1995; Sankaranarayanan, 1998). Other age-related changes are also known



https://doi.org/10.1192/bjp.176.4.400-a Published online by Cambridge University Press