Selenium Deficiency and Clinical Findings in Schizophrenia: A Common Thread

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Abstract

Low selenium levels can potentially explain many clinical findings evidenced in various schizophrenic populations. Low levels of selenium in conjunction with an environmental insult might be the cause of a form of schizophrenia. A problem in a hypothesized protein might possibly result in low selenium levels even in instances where selenium intake is generally deemed adequate. If the theory is correct selenium supplementation ought to prove an effective treatment in certain schizophrenic populations - populations defined by brain damage and negative symptoms.

Selenium and Schizophrenia

This paper argues that a problem in selenium biometabolism in conjunction with an environmental insult to the brain might be the cause of a form of schizophrenia.

I argue here that a problem in the biometabolism of selenium may well be a necessary step in the development of the disease in certain schizophrenic populations -populations defined by brain damage and negative symptoms. A possible problem in selenium biometabolism can explain many of the diverse clinical findings exhibited in schizophrenics. Too, I argue that selenium supplementation ought to benefit schizophrenics who present with low selenium levels.

This paper does not argue that a problem in selenium biometabolism exists in all schizophrenic sub-populations, nor does it argue that a problem in selenium biometabolism is, in and of itself, sufficient for the expression of the disease. (Selenium deficiencies might make an individual susceptible to viral infections. Keshan disease, a cardiomyopathy, is a disease associated with selenium deficiencies, and investigators of Keshan disease have speculated that the selenium deficiency might make the afflicted individual susceptible to a viral infection (Gu and Cheng, 1986). A subtype of schizophrenia might have a similar etiology.)

Selenium is a necessary mineral and it affects the activity of various enzyme systems -either as a component of an enzyme or as the selenium ion.

Researchers have argued that prostaglandin levels are abnormal in schizophrenia (Rotrosen and Wolkin, 1987). The exact nature of the disturbance, however, is not clear. Some researchers argue that prostaglandins are decreased in schizophrenia. For example, Linnoila et al. (1983) found no detectable levels of PGE2 and PGF2alpha in the schizophrenic patients they studied.

Scientific studies indicate that selenium ions have a potent inhibitory effect on the Inactivation process of PGE2 and PGF2alpha (Fugita et al., 1990). These researchers argue that selenium ions potentially can increase levels of biologically active prostaglandins. Selenium ions, then, can increase levels of PGE2 and PGF2alpha.

The findings of Linnoila et al. (1983) certainly are consistent with a selenium deficiency. Low levels of selenium would lead to the rapid Inactivation of PGE2 and PGF2alpha. Low selenium levels, then, can explain a clinical finding evidenced in schizophrenics.

Selenium is a component of the enzyme glutathione peroxidase, and low levels of selenium will decrease the activity of the enzyme. Glutathione peroxidase levels are decreased in individuals with low selenium levels. Glutathione peroxidase levels increase as selenium levels increase up to a saturation point (Rea et al., 1988; Lockitch, 1989; Lloyd et al., 1989). A linear correlation has been observed between whole blood selenium concentrations and blood glutathione peroxidase activity up to blood selenium concentrations of .100 g/ml. Above these concentrations the enzyme tends to plateau (Thomson et al., 1977).

Research indicates that low levels of glutathione peroxidase are in evidence in various schizophrenic populations (Abdalla et al.,

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1986; Buckman et al., 1987; Buckman et al, 1990). Buckman et al. (1987, 1990), claims that low levels of glutathione peroxidase are associated with negative symptoms and brain damage. Stoklasova et al. (1990) found only a slight decrease in the glutathione peroxidase levels of schizophrenic men, but in this study no breakdown by type of schizophrenia was attempted.

Glutathione peroxidase is an antioxidant enzyme and possibly low levels of this anti-oxidant enzyme can adversely affect dopaminergic neurons. Researchers have argued that free radicals might be involved in the etiology of Parkinson's Disease, a disease which, of course, involves dopaminergic neurons (Halliwell, 1989). See Bery (1992) for a discussion as to how low glutathione peroxidase levels might be involved in the etiology of a sub-type of schizophrenia.

A problem, then, in the biometabolism of selenium can explain the low glutathione peroxidase levels found in a specified schizophrenic population.

Selenium supplementation can improve mood in selenium deficient populations (Benton and Cook, 1991). This finding certainly is consistent with the point being argued.

States that have low levels of selenium in the food chain have high incidences of schizophrenia (Foster, 1988). Likewise countries known to be deficient in selenium have high incidences of schizophrenia. Norway and Sweden are known to be extremely deficient in the intake of selenium and Norway and Sweden both have high incidences of schizophrenia (Foster, 1990).

Finally, investigators recently have claimed that a selenium deficiency produces an inhibition of deiodination. Researchers claim that these data are consistent with the view that iodothyronine deiodinase enzymes are seleneoenzymes or require selenium containing cofactors for activity (Arthur et al., 1991; Nutrition Reviews 1991; Beckett et al, 1989; Beckett et al., 1987). A problem at this juncture affects the levels of thyroid hormones. A problem in the deiodination of T4 to T3 will increase levels of T4 and decrease levels of T3.

Schizophrenics often have abnormal thyroid hormone levels. Prange et al. (1979) researched this issue and they discovered abnormal levels of thyroid hormones. They claim that data they generated is consistent with the concept that in schizophrenic patients there is a reduced conversion of T4 to T3 in peripheral tissues.

As we have seen a reduction in the conversion of T4 to T3 is consistent with a selenium deficiency.

Possibly a protein might affect selenium levels even when selenium intake is adequate. Recently a new selenium containing protein has been isolated in rat plasma (Motsenbocker and Tappel, 1982; Burk, 1989). This protein, Selenoprotein P is thought to possess a transport function. Might the analogous human protein be involved in the etiology of schizophrenia? I suggest here that it might. Minimally, a protein that affects selenium levels ought to be involved in the etiology of schizophrenia - if not Selenoprotein P then another protein.

Implications

The theory makes several testable predictions.

1) Selenium levels will be found to be low in various schizophrenic populations.

2) A protein will be found in humans that affects selenium levels. This protein will be low in various schizophrenic populations and consequently measured selenium levels, too, will be low. If this protein has a low activity selenium levels will be low even though selenium intake is adequate. This protein will be found to be low in a disproportionately high number of schizophrenics. (A Protein that exists in abnormally high levels and which has the effect of greatly reducing selenium levels seems a less likely possibility, but cannot be excluded.) Possibly this protein is Selenoprotein P.

3) In certain instances the gene that codes for the hypothesized protein will be found to be defective, and consequently selenium levels will turn out to be low despite adequate intakes of selenium. The gene that codes for this protein will be found to be defective in a disproportionately high number of schizophrenics.

4) Selenium supplementation should prove to be helpful in schizophrenics who present with low selenium levels.

Conclusion

Low selenium levels can explain many of the clinical findings evidenced in various schizophrenic populations. Low levels of selenium in conjunction with an environmental insult could very well be the cause of a form of schizophrenia. A problem in a hypothesized protein might lower selenium levels even in instances where selenium intake is generally deemed adequate. Selenium supplementation might prove to be an effective treatment for a schizophrenic sub-population, possibly defined by negative symptoms and brain damage.

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