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LETTER TO THE EDITORS

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A proposed primate animal model of autism

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Abstract Based on the fact that thalidomide, at a certain point in human pregnancy, produces autism, we propose administering thalidomide to pregnant monkeys at an appropriate point after conception. The infant monkeys born after thalidomide treatment of the pregnant mothers should manifest aberrations in social vocalization and in socialization behavior. Histological analysis of their brains should reveal areas whose damage will lead to autism. This can then be produced stereotaxically in infant monkeys to allow the better determination of the relation of degree of damage in these areas to the severity of autism.

Key words thalidomide – primate animal model – autism

Introduction

At present, there is no good animal model of autism [1]. However, Miller et al. [2] pointed out that in human mothers who took thalidomide during pregnancy to avert nausea, their children became autistic with a much greater frequency than would have been expected from the usual incidence of autism in the general population. This fact provides the basis for the primate model of autism we propose here. Simply administer an appropriate dose of thalidomide to pregnant squirrel monkeys at an appropriate time in their gestation, and the same kind of brain damage that caused autism in humans should be produced in their infants. The autism should be manifested by the fact that these infant monkeys should avoid social contact, at a time when normal squirrel monkeys seek it [3]. Furthermore, since normal squirrel monkeys engage in a great deal of social vocalization [3], "autistic" squirrel monkeys should be deficient in their social vocalization as well.

Miller et al. [2] reported that the human mothers took thalidomide in days 20–24 of their pregnancy. The human gestation period is about 40 weeks (280 days). The gestation period in the squirrel monkey has been estimated at about 150 days [4]. If we take 22 days as the midpoint in the period when thalidomide ingestion in the human expectant mother resulted in autistic babies, then x:150 as 22:280 = about 12 days into a squirrel monkey mother's pregnancy. Therefore, we would expect that if an appropriate dose of thalidomide were administered to a pregnant squirrel monkey 12 days into her pregnancy, her offspring should manifest the symptoms of autism.

The advantages of such a primate model of autism should be very great. First of all, it would be possible to localize more precisely the areas in the brain whose damage produces autism. At present, areas in the cerebellum [5] have been suggested to be involved, based on MRI studies of the brains of autistic subjects. Cortical involvement has also been suggested [6]. Studies of autistic adults at autopsy have indicated that areas of the hippocampus and the limbic system may be involved [7]. Rodier et al. [8] have pointed out that brain stem areas involved with cranial nerves VI and VII may play a role in autism. Teitelbaum et al. [9] have suggested that responsivity to vestibular signals may also be deficient in a subgroup of autistic children, based on a deficiency in their head-righting response to simple body tilt. This would also indicate involvement of cranial nerve VIII.

Localization of the brain cells involved in autism should permit the stereotaxic destruction of these cells,

freeing the investigator from the use of thalidomide-induced destruction of them. This would allow more precise variation of the number of cells damaged, with expected correspondence in the degree of severity of the autism produced. We would expect movement disturbances to be apparent in the "autistic" infant squirrel monkeys, analogous to those reported in autistic humans in infancy [10]. It would be interesting to know whether a subgroup of such "autistic" monkeys would show deficiency in the head-righting response to lateral body tilt, analogous to that pointed out in the vestibular-deficient subgroup highlighted by the preliminary investigations of Teitelbaum et al. [9].

Obviously, an analogous procedure could be applied to other, more encephalized, primates, such as the rhesus monkey, as well.

Finally, such an animal model would permit the testing of the influence of the administration of vaccines such as the measles-mumps-rubella vaccine to see whether such vaccines in infancy can damage the brain cells corresponding to those damaged by the thalidomide-induced form of autism. This would help to settle the controversy that currently rages over whether such vaccines may cause autism or increase susceptibility to the factors that produce it [1].

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