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Review

Multiple sclerosis and certain neurodegenerative diseases are caused by high energy electromagnetic fields (EMF) like geomagnetic storms. A hypothesis.

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Abstract

The cause of multiple sclerosis (MS) remains unclear, although certain environmental factors have long been suggested. MS is predominant in areas where geomagnetic storms often occur. Migration of subjects before age 15 from low- to high-incidence areas increases the incidence, and vice versa, Moreover, those who migrated from a high- to low-incidence areas at age 15 or older retain the same risk of disease, suggesting that the conditions of myelin capacitance and plasticity by age 15 may determine the risk of developing MS. In addition, myelin is an electrolytic capacitor extremely vulnerable to high voltage electricity. MS has a statistically significant association with electrical injury. Furthermore, the earliest pathological finding of MS is primarily myelin breakdown, demyelination. Therefore when human brains are exposed to a high voltage electromagnetic fields (EMF) as in geomagnetic storms, myelin capacitors could be destroyed, particularly at sites of incomplete electric nonconductance of cell membranes. Another possibility is that the overcharged myelin capacitors may make nonphysiological repetitive or continuous over-discharges, which may leak electricity at unmyelinated nodes of Ranvier. As a result, demyelination occurs and transmission of action potentials becomes impossible. The impairment of cascades of the electrical and chemical signaling systems further causes degeneration or death of myelin, axons and neurons. In addition, a high energy EMF can produce a "hotspot" in the center of the brain, creating an increase in cerebrospinal fluid (CSF) temperature. Heated CSF could cause tissue degeneration both inside and outside the brain. Accordingly, MS lesions have two etiologic types, electric shock burn and hot water burn. The antigenic myelin debris might have been more or less modified by heating to an altered self, which will produce a different type of antibody in every MS patient. Since the antibody produced by an altered-self antigen may be unable to recognize the specific antigen, myelin, this could be why a common specific antigen remains unidentified in MS. Thus, high energy EMF such as geomagnetic storms could well trigger MS. Furthermore, the neurodegenerative process could be part of the pathogenesis of neurodegenerative disorders such as Parkinson's disease, motor neuron disease, and Alzheimer's disease.

Introduction

Multiple sclerosis (MS) usually occurs in adults between the ages of 20 and 40[1)2)]. The geographic distribution of MS patients varies, with the greatest prevalence being found in regions close to the poles,

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such as northern Europe, Canada, the northern United States, Australia, and New Zealand[1)-4)]. It has been shown that migration from a high- to low-incidence area before the age of 15 reduces the risk of MS[1)2)4)5)], conversely migration from an area of low- to high-incidence increases the incidence. Those migrating at age 15 or older tend to retain the risk level of the areas of their birthplace. Since the myelination has almost reached the level of maturation by age 15[5)], the conditions of capacity, nonconductance and plasticity of myelin may hold a key to the answer of this migration puzzle.

The high-incidence regions of MS have frequent geomagnetic storms, which can cause power outages as well as beautiful auroras. Electrical trauma has a significant positive association with exacerbation or the occurrence of new symptoms of MS[6)], suggesting that a certain relationship exists between electrical injuries and MS[7)]. Furthermore, a significant improvement in MS symptoms after protection from electromagnetic fields (EMF) exposure has been reported[8)]. Therefore, there seems to be a link between MS and geomagnetic storms or electrical trauma.

A high energy EMF could also produce a "hotspot" in the center of the brain, creating an increase in cerebrospinal fluid (CSF) temperature. Heated CSF could cause tissue degeneration along drainage routes at both inside and outside the brain. Soon after, microglia could respond to the myelin debris that has been altered and modified to varying degrees by heating. In addition, it has recently been demonstrated that mobile phone EMF could induce unequivocal morphological transformation of resting microglia into activated microglia in rat brains, due presumably to the activity of voltage-gated proton ion channels of microglia[9)]. The proton ion currents are extremely temperature sensitive and are larger and faster at higher temperatures[10)]. Indeed, the influence on microglia was microwave dose-dependent: the higher the energy, the more intense the response[9)]. Thus, innate immune cells such as microglia that possess proton ion channels will become more active under high energy circumstances.

Based on these findings, the author hypothesizes that high energy EMF, such as geomagnetic storms, can cause MS and that lesions are involved by two heterogeneous mechanisms, electric shock burns and increased CSF temperature. In addition, the mechanism of neurological dysfunction due to damage to the cascade of the electrochemical signaling system in MS can be extended to certain other neurodegenerative disorders such as Parkinson's disease, motor neuron disease (MND), and Alzheimer's disease, which have been reported following electrical injuries[7)11)].

Why migration age affects the incidence of MS?

The developing myelin sheath has better neural plasticity and shows better remyelination following an episode of demyelination. Furthermore, the myelin sheath matures almost completely by age 15[5)], when the potential of neural plasticity is decreased. Thus, the age of 15 could be a threshold for myelin plasticity, which can recover the electric capacitance and nonconductance without any significant loss. The recovery at age 15 or older may leave persistent damage in rebuilt myelin. Abnormally thin myelin sheaths will be more vulnerable to even weak energy EMF exposure. This might explain why those migrating at age 15 or older to low-incidence areas retain a high risk of MS for the rest of lives.

Why are infants or elderly persons suffering from MS rare?

The myelin sheath is composed of very compact and densely laminated oligodendroglial cell membranes and has a very large cell surface[12)13)]. Since the cell membrane is an electrical nonconductor, myelin acts as an insulator and prevents excitation and electrical leakage across the axon cell membrane, except for the unmyelinated nodes of Ranvier[12)13)]. Myelin also represents a very efficient electrolytic type capacitor in the brain. If the intensity of external energy is the same, the amount of energy storage in electrolytic capacitors is higher, the narrower the distance between intracellular and extracellular spaces, and the larger the membrane of nonconductance. Thus, fully mature myelin sheaths can store and generate energy more efficiently than immature ones. Immature myelin sheaths have much a wider distance between intracellular and extracellular spaces and much smaller membrane surfaces. This means that myelin in infants cannot store and generate excessive nonphysiological energy to disrupt myelin following exposure to a strong EMF energy such as geomagnetic storms. Thus, the rarity of MS in infants could be ascribed to the immaturity of myelination.

The onset of MS after age 60 is also rare[1)2)]. Because body fluids are generally decreased in elder peoples, this rarity may be related to the decreased amount of liquid electrolyte soaking the dielectric between myelin membranes. The decreased myelin capacitance may not have a potential to destroy myelin any more, even after being exposed to high voltage EMF.

Why MS lesions are common and early in the neck region?

At the spinal cord level, the proportion of white matter to gray matter decreases progressively from the cervical level to the sacral level[12)]. The population of myelinated nerve fibers could be the highest per area

diameter at the cervical cord level. Myelin sheath thickness correlates with axon diameter, i.e. the myelin sheath becomes thicker as the diameter of the axon increases[12)13)]. Moreover, motor neurons generally have large axons compared with sensory neurons. Thus, myelin capacitors of motor nerve fibers are able to store and generate more energy than those of sensory fibers.

On the other hand, electrolytic capacitors have well-known drawbacks such as poor tolerance, high leakage, and loss of capacity, particularly when subjected to high electric voltage. Moreover, many repeated overcharges may result in a rapid deterioration of the capacitance. The high capacitance areas can be more easily destroyed or overcharged, when exposed to a high external energy. Thus, MS lesions occur commonly and earlier in the cervical cord before involving the cerebral hemispheres[7)]. Moreover, the cervical cord is more commonly involved than the lower level[1)].

Why do MS lesions tend to be symmetrical ?

MS lesions are often said to be randomly scattered, but a careful study showed a distinct symmetrical distribution[7)]. A certain amount of CSF goes into brain parenchyma directly through the ependymal layer and into the perivascular spaces of fenestrated blood vessels of periventricular organs distributed widely around the ventricular walls. The remaining CSF flows out into subarachnoid space, bathing the entire surface of the brain. If a "hotspot" were created, the parenchyma adjacent to heated CSF flow would undergo degeneration. Normally, both drainage routes of CSF and conditions of myelination are the same in both hemispheres. Thus, it is reasonable that the plaques produced by high energy EMF would tend to be symmetrical. The lesions produced by electric shock burn may be small and scattered, while those by heated CSF burn could be more extensive and predictable in distribution. Moreover, the common involvement of optic nerves, brain stem and spinal cord could be explained by the anatomical proximity of the CSF flow. The extent and severity of the lesions may reflect the energy of EMF. The more severe and the wider the lesions are, the higher the EMF energy is.

Why has no specific antigen been identified in MS ?

The earliest pathological finding of MS is generally myelin breakdown, without any accompanying infiltrating inflammatory cells[7)]. Indeed, one-third of all MS cases have no perivascular lymphocyte cuffing[7)]. Although there is no definite immunological evidence to confirm that MS is an autoimmune disease[7)], an autoimmune hypothesis of MS has been widely accepted. If MS is indeed an autoimmune disease, why has no common specific antigen been determined in MS ? A possible answer is that antigenic myelin debris might have been modified by heating to an altered autologous substance, which would produce a wide variety of different types of antibodies in MS patients. Thus, an antibody in response to the altered autologous antigen in one patient would not be able to recognize the antigen, myelin elements, in another patient. This could be why no specific common antigen has been found in MS patients.

Why are there geographical and temporal clusters of MS patients ?

Endemic clusters of MS patients were observed in the Faroe Islands between 1938 and 1972[3)]. An infectious cause was considered but the etiologic agent remained unidentified. Another space-time clustering was found in Norway, suggesting again an exposure to infectious agent in adolescence, such as Epstein-Barr virus or a similar latent virus[14)15)]. However, no infectious agent for MS has yet ever been confirmed.

Concerning the data of strong geomagnetic storms in Japan for the last 80 years[16)], as many as 39 geomagnetic storms have been recorded at about the same period of years of the endemic clusters of MS patients in the Faroe Islands. Eight of them are in the top 10 strongest recorded. Since the Faroe Islands and Norway are located in higher latitudes, the storms must have had stronger energy. Therefore, geomagnetic storms might be a cause of the geographic and temporal clustering of MS.

Why has MS been progressively increasing in some countries ?

A highly significant and marked increase in incidence of MS has been noted over a 30-year period from 1953 to 1982 in Western Norway[14)]. Similarly, the number of MS patients has ever progressively increased during the 30 years period from 1974 and 2003 in Japan[17)]. The absence of temporal fluctuation or clustering in Japan suggests that an infectious cause is unlikely. The development of genetic changes is also unlikely among Japanese in such a short period of time.

On the other hand, there are rapid and progressive environmental changes, which are related to profuse development and growth of electrical appliances emitting various types of EMF during the same 30 years in Japan. Modern high-tech products are now ubiquitously present in homes, offices, and even outside on the streets where people are walking. Thus, the progressively ever-growing human-made EMF may have an important role in the ever-increasing number of MS patients in Japan.

Why do more women tend to suffer from MS?

MS patients are more common among women worldwide[1)2)]. The incidence of MS has continued to increase more significantly among women and the younger generation. In Japan, the peak age of incidence has decreased from the fourth to the third decade in the last 15 years for unknown reasons[17)]. The role of sexual hormones seems to be unlikely. Pregnancy affects MS but it is only temporary. There is evidence that the relapse rate of MS is reduced during pregnancy, particularly in the third trimester, and rises 3 months after birth, before returning back to the pre-pregnancy rate[18)]. An alternative and very attractive hypothesis of vitamin D deficiency among women has been proposed[12)]. However, it seems difficult to explain why there is a recent tendency for MS to increase in frequency, particularly among younger patients worldwide.

Women in general and the younger generations in particular have more chances to use a variety of electrical products close to the face or head for beauty care on a daily basis. This would result in a greater likelihood of human-made EMF exposure. Thus, it is possible that the more frequent usage of such products may be a major contributory cause to the universal female predominance of MS.

Why do radiation therapy or hyperthermia exacerbate the symptoms of MS worse?

The clinical worsening or appearance of new lesions of MS following radiation therapy[7)] might be ascribed to the fact that therapeutic radiation represents a part of the spectrum of EMF. However, the phenomenon of worsening MS by hyperthermia induced by hot shower, bathing or other means could basically have the same mechanism as MS lesions induced by increased CSF temperature.

Irradiation causes the destruction of the blood-brain barrier (BBB), contributing to the development and worsening of MS lesions[7)]. The BBB must be destroyed in MS lesions of both electric shock burn and hot CSF burn, too.

What EMF could cause MS?

Certain non-ionizing EMF, such as sunlight and microwaves can pass through various protective barriers present between the earth and the cosmos. Sunlight exposure during childhood and early adolescence appears to have a protective effect against the development of MS[12)], indicating that sunlight is an unlikely cause of MS. On the other hand, microwaves reach the earth in varying amounts together with wide varieties of EMF due to geomagnetic storms too. As shown in an experimental study[9)], microwaves have a definite influence on the brain. Thus, microwaves could be a risk of EMF for living creatures and have a potential to cause MS.

Effects of genetic factors in MS

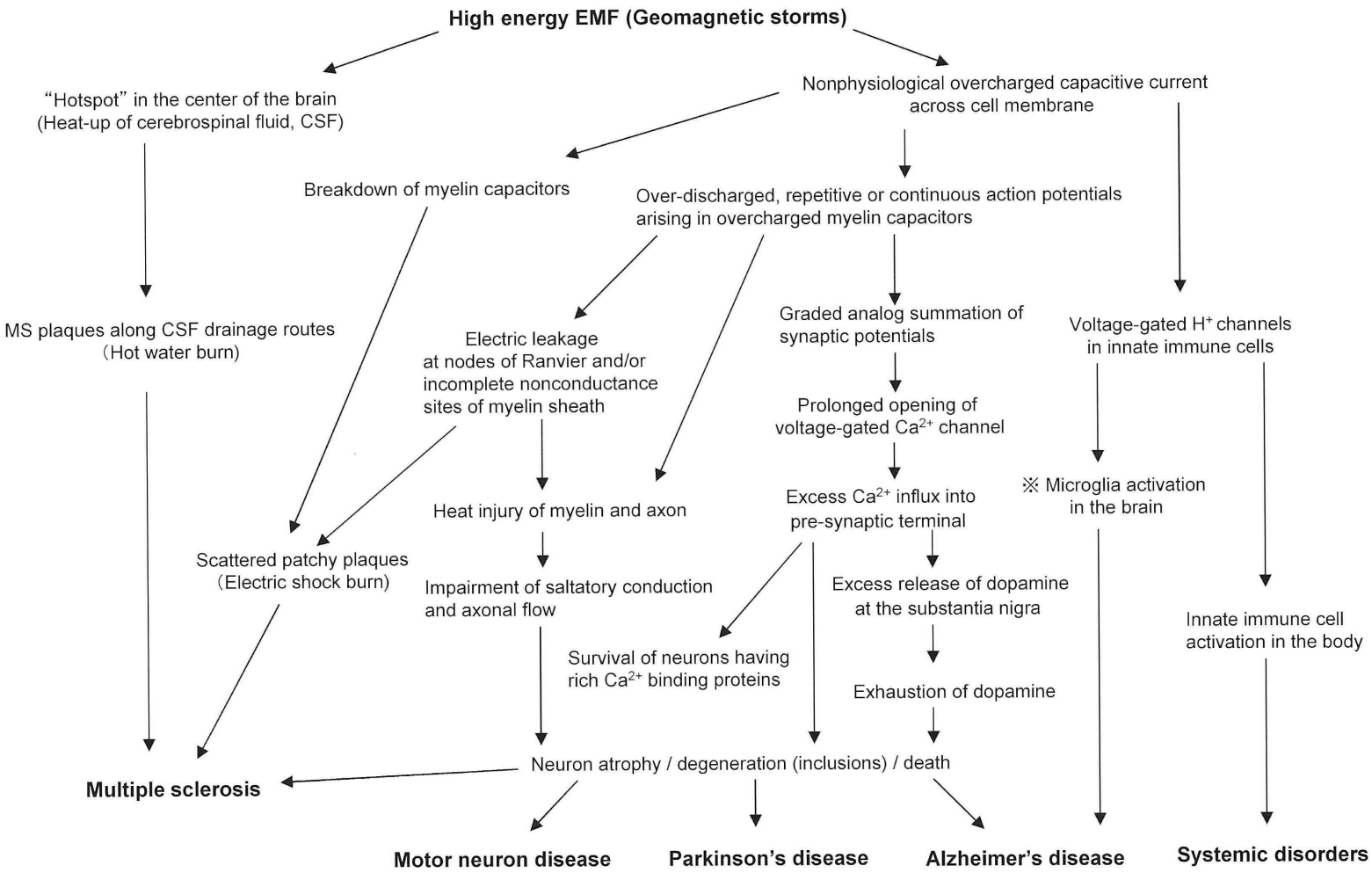
Racial differences in the prevalence of MS have been reported[2)4)7)]. In addition, the risk of MS is increased 15 to 20-fold in the first-degree relatives of MS patients[2)]. Also, the concordance rate of MS is significantly higher in monozygotic twins than in dizygotic twins[2)7)]. Moreover, a link to chromosome 17 has been emphasized[2)7)]. These data indicate that certain genetic factors must be involved in MS, as in many other disorders described in this article. Therefore, there is no question that genetic factors contribute to the development of these neurological disorders in some way or another.

Why is MS often associated with certain neurodegenerative disorders?

Normally, a series of all or none digital action potentials that are generated in axon hillocks of neurons are rapidly conducted along the nerve to spread to all other parts of the cell[12)13)]. However, if the nerve is non-physiologically or artificially stimulated at the periphery or the middle part, the conduction will spread in a retrograde direction towards the cell body or in both directions[12)]. Thus, neurological dysfunctions due to the impairment of cascades of the electrical and chemical signaling systems after strong EMF exposure could vary considerably, depending upon many unknown factors including the direction and destination of nerve impulses. Moreover, very interestingly, these neurological disorders have a statistically significant association with electric injuries[6)7)] and have been reported in occupational exposure to extremely low frequency EMF[12)]. Furthermore, EMF can activate microglia[10)] and the microglia are believed to play a role in the pathogenesis of various neurodegenerative and neuroinflammatory diseases, including MS[23)]. Thus, neurodegenerative changes in MS[19)] and certain neurodegenerative diseases could have a common pathogenesis, as shown in Figure 1.

1. MND

The strong tendency of motor nerve involvement in MND is only a relative matter. Indeed, extra-motor involvement is becoming increasingly apparent in MND[1)2)]. Capacitor overcharge tends to happen in motor nerves with thicker myelin following strong EMF exposure. The electrical action potentials are converted into chemical signals at synapses. Synaptic potentials are graded analog signals and vary in proportion to the size of stimuli. The summation of synaptic potentials can generate new action potentials repetitively at the postsynaptic terminals[13)14)]. Action potentials at synapses open the voltage-gated Ca^{2+} channels, which are



※ Microglia also play a role in the development of other neurological diseases described herein.

Fig. 1 Exposure to a strong energy EMF such as geomagnetic storms could cause MS lesions of two different types, electric shock burn and hot water burn. And, the neurodegenerative process could be part of the pathogenesis of MND, Parkinson's disease and Alzheimer's disease.

energy-dependent. The effects of summation of multiple over-discharged impulses from overcharged capacitor will result in excess influx of Ca^{2+} into neurons through repetitive or continuous opening of Ca^{2+} channels. Excessive calcium influx may induce apoptosis or necrosis of neurons. However, certain motor neurons in the cranial nerve nuclei, such as in the oculomotor, trochlear, and abducent nuclei, are relatively spared in MND[1)2)20)21)]. The spared motor neurons possess more Ca^{2+} binding proteins, which can sequester the excess calcium[20)21)]. Therefore, neurons poor in Ca^{2+} binding protein will undergo cell degeneration or death via an excitotoxic pathway, leading eventually to atrophy and death of lower neurons and muscles. Moreover, protein-rich motoneurons could resist the excess calcium influx.

2. Parkinson's disease

The influx of Ca^{2+} through the Ca^{2+} channels stimulates the cells to secrete and synthesize the neurotransmitter[12)13)]. However, a prolonged opening of voltage-gated Ca^{2+} channel causes over-release of dopamine at synapses in substantia nigra, leading eventually to exhaustion of dopaminergic substance. Likewise, Ca^{2+} binding protein rich dopaminergic neurons are relatively spared[21)]. Microglia also play a role in the pathogenesis of Parkinson's disease[24)].

3. Alzheimer's disease

Microglia are also believed to play a role in the pathogenesis of Alzheimer's disease[23)24)]. Thus, EMF also has the potential to cause Alzheimer's disease.

Predicting the future of MS and certain neurodegenerative disorders

The occurrence of geomagnetic storms is closely related to the solar cycle that rises and falls every 11 years[25)]. There is a forecast that the solar cycle in 2010 or 2011 is going to be one of the most intense since record-keeping began almost 400 years ago[25)]. If indeed strong EMF such as geomagnetic storms can cause MS, a cluster of MS patients would be observed soon after the year 2010 or 2011. It may be possible to quantify the minimum amount of EMF energy needed to cause MS. Moreover, time clustering of MS might have average transmission intervals of 11 years or so.

If the rapid global increase of human-made EMF continues, MS patients may spread diffusely worldwide, including areas where MS is still rare at present. In addition, the geographic and temporal clustering may become indistinct. On the contrary, protection from EMF exposure may result in a decreased incidence of new patients and temporary improvement of symptoms[8)]. In addition, sunlight exposure during pregnancy and childhood and vitamin D supplementation in adults diminish the risk of MS[5)7)].

EMF could cause innate immune related systemic diseases too.

Since mobile phone EMF activate microglia that belong to innate immune system and are most potent antigen-presenting cells in brain[9)], EMF could theoretically activate other various innate immune cells circulating in blood and residing widespread in various organs and tissues throughout the body[9)]. A stereotypic response of these innate immune cells includes phagocytosis, antigen presentation, and secretion of a variety of immune factors that orchestrate an innate immune response and recruit various inflammatory cells to injured tissues, which may further induce an acquired immune response[22)-24)]. Thus, EMF could cause a wide variety of systemic immunological dysfunctions and the related disorders such as autoimmune diseases and tumors.

Conclusion

The effects of EMF on myelin electrolytic capacitor, CSF and electrochemical signaling system of the brain have been completely ignored as a possible cause of MS and other intractable neurological disorders of hitherto unknown etiology. Thus, I believe we need to drastically change the paradigm for the study of MS and other neurodegenerative disorders.

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多発性硬化症やある種の神経変性疾患は強い電磁気暴露により発症する —仮説—

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多発性硬化症の原因は未だ不明であるが、その発症には環境要因が深く関わっているとされる。患者は、北米、北欧、豪州やニュージーランドなど、極地に近い、しばしば磁気嵐が発生する地域に多い。高頻度地域の住人が15歳になる前に低頻度地域に移住すると、新しい土地の罹患頻度に従い低くなる傾向がみられる。その逆も真なりである。そして15歳以後の移住では生まれ育った土地の頻度を維持し続ける。つまり、本症を発症する危険度は15歳までの髄鞘の形成度合いやその可塑性がある程度規定していると考えられる。興味あることに、髄鞘は、構造的に電気的に電解質性蓄電装置であるゆえ、高電圧の曝露には極めてもろい組織と考えられる。統計学的に本症は電撃的外傷と有意な因果関係にあると指摘されている。そして、病理学的に本症のごく初期像は髄鞘破壊、つまり脱髄である。したがって、磁気嵐のような強い電磁気に脳が曝されると、髄鞘は、特に絶縁体の不完全部分で破壊される危険があるだろう。たとえ破壊されなくとも、過充電により加熱された活動電流が髄鞘を欠くランビエ絞輪部で、あるいは絶縁体機能の不完全な髄鞘形成期の小児では髄鞘部分でも漏電する危険がある。また活動電流が繰り返し頻発し、ついには持続放電を起こす可能性がある。その電気化学信号系統障害により次第に有効な活動電位の発生や伝播も不可能になると考えられる。その一方で、強い電磁気の発熱作用は脳中心部にホットスポット現象、つまり脳室内髄液の温度上昇を生ずる。その結果、加熱された髄液の吸収・排出経路に沿う組織は変性・破壊される危険がある。したがって、本症の病巣形成には電気ショックと温水熱傷の二通りの経路が関与していると考えられる。その自己（髄鞘）由来の抗原は熱でさまざまな程度に修飾・変性された非自己成分をもつため、産生される抗体には患者毎にかなりの相違が生じるだろう。このことが、本症の患者間に共通抗原を確認同定できない最大の理由であると考えられる。つまり、自己免疫疾患説で特異的自己抗原が確認できないのは、患者一人ひとりの髄鞘が熱で多種多様に非自己に改変された抗原エピトープ部分を持つためと考えられる。なお、多発性硬化症における神経変性機序は、パーキンソン病や運動神経疾患、そしてアルツハイマー病などの神経変性疾患にも適用しうるだろう。

〈キーワード〉 多発性硬化症、電磁気、髄鞘、電解質性蓄電装置、神経変性疾患