Does the Brain Regulate the Immune Response?

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Brain transection in the rat produced marked atrophy of the thymus with no remarkable changes of
the adrenals, lymph nodes and spleen in macroscopic and microscopic studies. However, the rat
which had no feeding as an experimental control showed no changes of the lymphatic system com-
paring in the normal sibling rats.

It is suggesting that the brain appears to play a role in immune reaction.

(Key Words: Immune Response, Immune System, Brain Immuno-Neuro Interaction)

The thymus is known to be a central organ with an important function in
cellular immunology. The central nervous system appears to regulate the
endocrine system and the immune system (2,3,4,6). The central nervous
system regulating of the endocrine is well-known (7) but there have been
few reports concerning the effect of the brain on immunity. The hypothesis
that complex relations exist among the nervous system, the endocrine
system and the immune system has been proposed (1,2).

We propose the hypothesis that there is an immune regulating system in
a higher level of the brain rather than in the thymus, and investigated the
effects of brain transection on the immune system in rats.

Approximately seventy male Wistar rats, weighting 250—300gr, were
used. Four experimental groups were arranged as follows: 1) Group I —
rats with completely transected brains, otherwise treated the same as those
in Group II; 2) Group II — rats which were given 20ml of milk each day per
os as an experimental control for stress and malnutrition; 3) Group III —
sham operation rats, otherwise treated the same as those in Group II; and
4) Group IV — untreated rats. Brain transection was performed using a
stereotaxic procedure according to a method of SZENTAGOTHAI et al.
(9) at the tentorial level under 50 μg/Kg of sodium pentobarbital anesthesia
given intraperitoneally (Fig. 1). All rats were injected intraperitoneally with
2 × 10⁸ washed sheep red blood cells, on the 1st and 3rd days after the pro-
Sera were collected by retrooccipital sinus puncture and used for kinetic studies of the immune response against sheep red blood cells. The rats were sacrificed on the 4th, 7th, 15th and 21st days after the procedure and the thymus, spleen, mesenteric lymph nodes and adrenals were examined macroscopically and microscopically.

Fig. 1  Sagittal section of the rat brain shown in the transected area

AC: anterior commissure  CO: chiasma opticum
GCC: genu corporis callos  HI: hippocampus
Hy: hypophysis  Th: thalamus

The kinetic analysis of the primary immune response showed that Group I responded in the same way as other groups but was delayed on day 1 and showed a slightly low titer (Fig. 2). The thymus and the spleen weights were markedly decreased in Group I but the adrenals showed no remarkable weight changes in any group (Fig. 3).

The thymus showed a profound depletion of lymphocytes, drastic reduction of the cortex and disappearance of the corticomedullar junction on the 4th, 7th, 15th and 21st days after the procedure in Group I. The spleen showed depletion of lymphocytes and decreased germinal centers in the remnants of the Malpighian bodies in Group I.

The lymph nodes showed a depletion of lymphocytes, disappearance of primary and secondary lymph nodules and disappearance of the germinal center in Group I.

In Groups II and III, only a slight depletion of lymphocytes was observed in the thymus but the adrenals showed no remarkable changes in any of the groups.

In previous reports, diminished immune responses of hypothalamus lesioned rabbits and rats were described (2,4,8). Our study indicated a marked involution of the thymus and peripheral lymphoid tissue similar to that observed by others (2,3,4). It must be assumed that the stress induced by brain transection may affect an immune suppressive action due to increased secretion of adrenal steroid. However, there was no remarkable change in the adrenals in macroscopic and microscopic findings. It has been reported that malnutrition or abnormal metabolism induces immune response depression (5). In our study, Group II, which was subjected to malnutrition
and altered metabolism, showed only a slight change in the immune system and recovered rapidly.

Brain transection may damage not only the neural feedback system in the neuro-endocrine system, if it exists. It may also influence the thymus, and the lower level, peripheral lymphoid tissue was regulated secondarily by the thymus. A delay in sheep red blood cell hemagglutinin formation may have a secondary influence by brain transection. Further studies concerning the neuro-immune system with respect to antigen recognition and the memory system, the antibody formation system, cellular and humoral systems, hormonal system, autonomic nervous system and others will be necessary.

![Fig. 2 Kinetics of hemagglutinin formation in Group I (●) and Group II~IV (○) after the procedure](image)

![Fig. 3 Changes of thymus, spleen and adrenals weights after the procedure](image)
REFERENCES


