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Alterations in Neuronal Development under Influence of Conditions of Nurture and Heterotopic Transplantation

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(1) Impoverished nurture created through undernutritional condition caused significant deviations in the dendritic arborization and numerical spine densities of pyramidal neurons of visual and motor cortices in developing rat brain. The development of spine numbers lagged behind in the initial postnatal ages, but later on the numbers increased and continued at a level higher than the control without having been pruned while attaining the adult age. This was interpreted as a homeostatic adaptation response of the neurons in the brain to the demands of undernourished state. (2) The enriched experience provided through operant learning sessions in the normally nourished developing rat pus also caused certain increments in the spine densities of specific regions of dendrites of hippocampal CA3 neurons, i.e., implying that only some inputs to the neurons might have been involved in providing the stimulus for the spine genesis in the developing brain. (3) The hippocampus transplant that matured under heterotopic environmental conditions showed significantly reduced spine densities as well as dendritic branching, in yet another manner. However, several of these grafted pyramidal neurons have more exuberant branching of apical dendrites and high spine densities, even better than the native control, while the basal dendrites showed the opposite trend of development. Hence the alterations in the transplants may not be simply due to the effect of a new environment, but may be due to complex interactions of both growth promoting and pruning factors within the neurons and without. (4) Thus, the three models of experimentation revealed the scope and variety of alterations of the neuronal phenotypes being the products of expression of the genetic and epigenetic or environmental influences.

Key Words **Developmental neuronal plasticity, Nurture moulding neurons, Neural transplants, Learning and neurons, Brain growth under undernutrition**

Introduction

In recent years, knowledge on the factors that alter the development and maturation of neuronal connections and synapses has been rapidly advancing. It has been revealed that there is a significant degree of plasticity in the shaping of neuronal connectivity. The studies presented in this paper contribute information from experimental model approaches to assess the modifiability of dendritic branching and spine genesis of cerebral cortical neurons (both neocortex and limbic cortex), by varying either the material conditions of nurture (diet restriction) or by varying experiential opportunity made available to the subject during the age of brain growth and development. Further more, this report also presents information from another model of study on the type of changes that might occur in neurons when neural tissuses are transplanted from their native region into new sites of nurture. These studies are intended to advance the understanding of the conditions that induce the expression of plasticity of neurons as well as the nature of the response.

Materials and Methods

All the experiments have been done on Wistar rats. The details of the methods of nutritional deprivation and assessment of resulting alterations of dendritic arborizations and spine numbers of neocortical pyramidal neurons have been described earlier (Gundappa & Desiraju 1988, Mascarenhas et al. 1986, Rajanna et al. 1987). The method of providing new or enriched experience through operant conditioning and assessing consequential changes of dendritic branching and spine densities of hippocampal pyramidal neurons was described in detail earlier (Mahajan & Desiraju 1988). The methodological detail of transplantation of embryonic hippocampal neural tissue into neocortex of juvenile recipient, and the assessment of the changes of dendrites and spines of neurons in the grafted tissue was also published earlier (Murthy & Desiraju 1989). The method of electronmicroscopic analysis of alterations of synapses in EPTA treated cortical tissue has been also described elsewhere (Murthy et al. 1989).

Results

Deprived (nutrition) condition: The ontogenetic processes of exuberance and pruning of dendritic spines of pyramidal neurons of neocortex (lower laminae of visual and motor areas) were firstly characterised in rapid Golgi studies in developing Wistar rats reared under normal conditions. Secondly, the effect of changing the condition of nurture by depriving nutrition (caloric) during gestational and post-natal age was also studied (Gundappa & Desiraju 1988).

In the ontogeny of normally nourished group, exuberant spine densities (numbers) reached between 26-50 days of age and underwent a progressive decline or pruning upto about 50% by adult age, having certain differences among different categories of dendrites (basal, apical), and between visual and motor cortical neurons. The patterns of ontogenetic changes of the neurons of undernourished group were also similarly assessed and compared. The undernourished neuronal ontogeny was significantly altered, in that there was an initial lag in the spine densities, followed by an increase in the spine densities which continued upto the adult age, instead of the normally expected pruning. This deviation in the pattern due to deprivation in nurture during the early age could not be prevented by late postnatal restitution of normal nutrition. Number of the EPTA stained synapses in the molecular layer of the undernourished rat brain cortices also showed similar patterns of deviation (Murthy et al. 1989).

Learning experience: In another experimental approach, enriched experience was provided to 18-day old rat pups in operant conditioning paradigm for food reward for a few days, and the changes of dendritic branching and spine densities of hippocampal pyramidal neurons of CA3 region were assessed. The data revealed significant increases in the dendritic branching of the hippocampal neurons and spine densities of some specific segments, thereby showing that the enriched experience altered neuronal development (Mahajan & Desiraju 1988).

Transplant Development: In another approach of study, embryonic (18-day) hippocampal tissue was transplanted into neocortical cavity in 18-day-old rat pup to study the extent of differentiation and development of neurons in a heterotopic environment. Such a study was expected to contribute to the understanding of the scope of plasticity in neuronal development (Desiraju 1989). The results showed that the hippocampal neurons (granule and pyramidal cells) developed apparently normal forms, but with significantly reduced dendritic branching and spine densities in some neurons compared to native hippocampal neurons (Murthy & Desiraju 1989). There were also aberrations in the forms of neurons, The basal dendrites of the CA3 neurons had significantly less branching and spines than control, while the opposite trend of exuberence was observed with apical dendrites.

Discussion

The above studies revealed that the differentiation and development of cortical neurons can be significantly altered in different ways by different conditions of nurture. They have a wide range of plasticity. In the subjects nurtured on undernutrition, the computerized electrographic power spectral analysis revealed major deviations from normal (Rajanna et al. 1987). The levels of dopamine, noradrenaline and serotonin of different brain regions of these subjects were also significantly

altered (Annamma and Desiraju 1988). Hence, it was obvious that the undernutritional nurture caused significant alterations in not merely the cortical pyramidal neuronal dendrites, but in the larger networks of the developing brain. These are probably homeostatic adaptation responses. Alterations in the neurotransmitter content of different brain regims (dopamine, noradrenaline, serotonin, glutamate and GABA) were also observed in the brains of rats consuming lead during postnatal brain development (Shailesh Kumar & Desiraju 1990).

The increase in number of spines in specific regions of dendrites in learning experiments indicated that transmission was augmented for some afferent inputs due to tenriched early learning. The transplanted neurons having been disrupted of afferent connections responded in a different manner.

From the observations it is clear that the various conditions of nurture, both of material kind and of subjective experimential kind will critically determine the shaping of the brain neural networks and their functioning perhaps within the limits of genotypic possibilities of individuals. In the foreseable future, further informations in this area will lead to development of special applications that can enable to mould the growth and expression of the potentials in each individual, and also to prevent maladaptations or to devise appropriate therapeutic methods to correct some of the ills.

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