
Crowding Stress

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GLOSSARY

amyloidosis A severe pathological change of various organs and tissues where aggregated amyloid fibers develop and induce the destruction of affected cells.

channeling Interaction of enzymes catalyzing consecutive enzyme reactions where the product of the "first" reaction becomes the substrate of the "second" enzyme by a directed molecular transfer largely avoiding free diffusion.

hypothalamic-pituitary-adrenal (HPA) stimulation/axis A major peripheral mechanism of the stress response, involving three major constituents: the corticotrophin releasing hormone (CRH), corticotrophin (ACTH), and glucocorticoids.

molecular crowding A term to denote a dense population of molecules (usually macromolecules) where aggregation, diffusion, hydration, and other properties of the individual molecules are significantly altered.

Crowding stress is a type of psychosocial stress induced by an increased density of population. Population density may be raised either by increasing the number of species living in the same area and/or by reducing their living space. Crowding stress induces complex changes at the behavioral, physiological, and molecular levels, which differ, depending if crowding stress is acute or chronic. Crowding stress can also be interpreted at the molecular level: molecular crowding promotes aggregation of various macromolecules and causes profound changes in numerous physicochemical parameters of their solution.

I. INTRODUCTION

As outlined above, studies on crowding stress consider an exceptionally high number of variables. Several consequences of crowding stress may differ greatly, depending if population density is raised by increasing the number of species living in the same area or by reducing living space. If crowding is increased to such an extent that it leads to confinement, malnutrition, or an increased incidence of infections, other complications develop. Crowding stress may be "acute" (transient), i.e., the effects manifest after a few days, or "chronic," i.e., changes occur after prolonged overcrowding lasting for weeks, months, or even years. While mice or rats are the most commonly used species in crowding stress experiments, studies have been performed with almost all types of domesticated animals, various fishes, and even humans. Though the conclusions of these studies can be directly compared only within the same species, some general trends can be observed. This article focuses on these general aspects of crowding stress.

II. CROWDING STRESS: PSYCHOSOCIAL EFFECTS

Crowding as a chronic source of stress constitutes a major threat to psychological well-being. Dense populations are characterized by considerably increased aggressive behavior. Crowded monkeys (even well fed), including females and young, have brutal fights and wound and kill each other. Crowding stress adversely affects gonadal functions and if it occurs during pregnancy may inhibit reproductive activity of the second generation through masculinization of female pups. Chronic crowding leads to deficits in learning tasks and has been used in animal

models to induce depression. In human populations crowding stress is proposed to be an important factor in the development of increased urban insanity/schizophrenia.

III. PHYSIOLOGICAL CHANGES IN CROWDING STRESS

Crowding stress (especially if chronic) suppresses immune functions. Disturbed immune regulation leads to increased autoantibody levels and may be one of the factors behind the increased occurrence of childhood asthma. Various infections and increased susceptibility to poisoning are more likely to occur under crowded conditions. A widely established example indicates that household overcrowding is related to an increased prevalence of ulcer-inducing *Helicobacter pylori* infections. *Helicobacter pylori* infections and stress-induced gastric lesions significantly contribute to the development of ulcers and stomach cancer. Due to digestive problems and occasional appetite loss chronic stress induces weight loss. In several organs, such as in kidneys and adrenals, chronic crowding stress induces intensive amyloidosis. Chronic overcrowding in many cases leads to hypertension in the resting state or to "relative hypertension" after exercise.

IV. POSSIBLE MOLECULAR MECHANISMS OF CROWDING STRESS

Crowding stress considerably impairs central histamine, noradrenaline, and vasopressin production but does not change the corticotrophin releasing hormone (CRH) system, which is involved in hypothalamic-pituitary-adrenocortical (HPA) stimulation. This is possibly the cause of decrease in appetite and consequent weight loss. Hypothalamic-pituitary-adrenocortical stimulation leads to compromised immune function and suppression of gonadal functions. Chronic HPA stimulation may lead to osteoporosis, chronic gastrointestinal pain, and retarded growth. Thus prolonged activation of the hypothalamic-

pituitary-adrenocortical axis may explain many of the psychological/physiological symptoms resulting from chronic overcrowding, such as gastrointestinal problems, weight loss, sensitivity to infections, and decreased reproductive activity.

Crowding stress may impair cellular signaling mechanisms, such as changes in intracellular calcium levels, especially in elderly subjects. Impaired signaling may significantly contribute to immune suppression and decreased adaptive mechanisms.

V. CROWDING OF WORMS

The signaling mechanisms can be studied more easily in simple organisms. The fruit fly *Drosophila melanogaster* ceases to develop in overcrowded cultures. Food limitation and overcrowding also induce arrested development of the worm *Caenorhabditis elegans*, leading to the formation of the so-called "dauer larva". Daf-7, a homolog of the human transforming growth factor- β (TGF- β), prevents dauer larva commitment. Several other members of the dauer larva regulating Daf family are receptor serine-threonine kinases similar to the human TGF- β receptor. Mutations of another signaling pathway of *C. elegans* may quadruple the adult lifetime of the worm besides disturbing its dauer larva development. Thus, disturbances in signaling due to crowding stress may have profound consequences in the longevity of (simpler) organisms.

VI. MOLECULAR CROWDING

Crowding induces changes in the "behavior" of macromolecules as well. If the total volume of a macromolecular species occupies a significant fraction of the total volume of the solution we refer to such a medium as "crowded." Under experimental conditions molecular crowding is induced by polyethylene glycol or by dextrane. An intracellular environment where the total amount of macromolecules usually occupies more than one-third of the total volume is a typical example of molecular crowding.

Positively, molecular crowding induces an increased association of macromolecules, enhancing channeling between enzymes catalyzing consecutive enzyme reactions or improving signaling efficiency in organized signaling cascades.

Yet at such a high density macromolecules begin to compete for water molecules, their hydration becomes compromised, and, consequently, osmotic stress occurs. The large amount of macromolecules and their immobilized hydrate shell constitute a large "excluded volume" which requires significant adjustments in physicochemical kinetics and equilibrium of various intracellular processes.

See Also the Following Article

INDUSTRIALIZED SOCIETIES, STRESS AND

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