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Neuroimmune Pharmacology as an Emerging Curriculum for Pre-Medical Students

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Abstract

As science continues to evolve and expand some major areas of interest are now crossing boundaries to become multi-disciplinary in nature closely reflecting the biological processes of the organism as a whole. The fields of neuroscience, immunology, and pharmacology are good examples of one such emerging inter-disciplinary area. This article is focused on developing a curriculum for undergraduate pre-medical students in the area of neuroimmune pharmacology (NIP) to empower them with the knowledge of neuroscience and its interaction with immune responses and drug interactions. This course is intended to amalgamate and put into perspective a large body of knowledge including: (1) brain function in health and disease, (2) cross talk between neural and immune responses, and (3) the pharmacology of drugs of abuse in the context of neurodegenerative diseases. The goal of this course is to expose pre-medical students to the field of NIP so that they are equipped with a solid foundation in these multidisciplinary fields for future clinical/academic careers.

Keywords

neuroscience; immunology; pharmacology; cytokines; chemokines

Introduction

Brain-related disorders account for the majority of long-term healthcare costs and hospitalizations more than almost all other diseases combined with almost one in four Americans affected annually by some or the other brain disorder. These comprise Alzheimer's disease and other dementias, alcoholism, autism, bipolar disorder, serious brain injury, drug abuse, mood disorders, strokes, and schizophrenia. It is thus not surprising that interactions among various fields related to these disorders is reshaping the landscape of neuroscience while necessitating multidisciplinary training of a new generation of students in the areas of neuroscience, immunology, and pharmacology as an approach to gain a more complete understanding of neuroscience in health and disease.

Advances in these multidisciplinary fields may also prove valuable in our approach to the treatment of substance abuse as these findings will provide insight into how drugs of abuse affect the brain leading to addiction. In addition, because some of these drugs, such as opiates, are routinely used for pain management, their chronic use in the context of neurodegenerative disorders could have paradoxical deleterious effects on the CNS. Research in this area can thus have clinical implications for healthcare practitioners. These studies may also help produce effective treatments for chemical dependency and help us to understand and prevent the harm done to the unborn children of pregnant women who abuse drugs and alcohol. Because there is a cross talk between the nervous and immune systems—the “mind–body connection”—studies of the brain may also enhance our understanding of acquired immune deficiency syndrome.

Neuroscience and immunology are two of the fastest growing fields of knowledge in the medical sciences. The global explosion of neuroscience research and the cutting edge, state-of-the-art technologies emanating from these fields, are driving groundbreaking advances in the fundamental understanding of both normal brain function and the pathological mechanisms underlying various neurological disorders. In fact, the age of neuroscience over the past two decades can be attributed primarily to the surge in scientific discoveries and advances in the diagnosis and treatments of common neurological diseases as well as increased public (stem cell debates) and federal (1990–2000, *Decade of the Brain*) awareness and support. The outcome measures of this growth have been reflected by dramatic increases in attendance at the Society for Neuroscience annual meeting, with 500 members at its inception in 1969 to over 40,000 members today. A parallel and dramatic blossoming of publications, new journals, and lay news articles in the field has also been evident. Concomitantly, there has also been an exponential increase in the number of neuroscience departments, programs, and courses at the undergraduate levels (Boitano and Seyal 2001; Ramirez 1997). Intriguingly, between 1980 and 2000, the number of undergraduate neuroscience programs or departments has more than doubled. Most primarily undergraduate institutions now have neuroscience courses from both the biological and psychological perspectives.

Basic description of the course

Objectives

This course introduces pre-medical students to the rapidly growing field of neuroimmune pharmacology, which is the study of the biology of the nervous system and its relationship to disease, immune system, and pharmacology. The course covers topics ranging from basic neuroscience (consisting of introductory neuroanatomy and cell types of the CNS, neuronal structure and function, apoptosis/necrosis (Hawkins and Davis 2005), cytokine/chemokine communication, signal transduction, blood brain barrier (Elmore 2007), and pathophysiology of neurodegenerative disorders) to neuroprotective mechanisms, the immune responses in the CNS, and the interaction of drugs of abuse with the pathological processes in the brain. Although the course is introductory in nature, emphasis will be placed on the convergence of signaling pathways in disease processes and on the common neuroprotective factors that can be developed as therapeutic targets. A major goal of this

course is to offer the student the essentials in the area of neuroimmune pharmacology (NIP) and to introduce current research topics upon which a more comprehensive knowledge of experimental investigation can be based. These topics will be covered in a format that exposes students to critical thinking, problem-based learning, and the two-way research-oriented teaching format.

Lectures

Didactic lecture sessions should be about 45 min long, 3 days per week. Informal study groups will be encouraged on a weekly basis to assist in the understanding of the lecture material. In addition to lectures, there will be three “Special Topics” lectures scheduled in which either visiting seminar speakers or faculty working in the neuroscience field will be invited to introduce their respective research that goes on in their laboratories. These will be informational lectures to familiarize the students with the new advances and development in the area of neuroscience.

Seminars in neuroscience

In addition to didactic lectures and special seminars, student pairs will present to the class a 60-min research seminar on a topic encompassing both the basic and clinical aspects of a particular neurodegenerative disorder with emphasis on immunology and therapeutics. There will be a 25-min time slot for basic and clinical topics, which will then be followed by 10 min of question–answer session. Students will be evaluated on their presentation, choice of article, and discussion. Students will also read and lead discussions of issues of general professional concern: peer review and the evaluation of research, the function of federal research agencies, science education and teaching. This will prepare them for a future career in either academia and/or clinical practice (Table 1).

Topics emphasized

Biology of mental disorders

Remarkable progress has taken place over the past two decades in our approach and understanding of syndromes often categorized as “psychiatric disorders” or “mental disorders”. To date the brain is still envisioned as a “black box” and there remains a paucity of therapeutic options to treat these disorders. However, there has been an increasing interest in understanding the molecular mechanisms of mental health and disease with the result that significant progress has been made for patients with these disorders. The underlying principle of this course is that there is a two-way cross talk between the brain and the periphery that impairs the mind–body connection leading to increased disease pathogenesis.

The first part of the course will cover basic concepts of neurobiology with an introduction to brain anatomy, cell types of the CNS, cytokine/chemokines, and the BBB. The second part of the course will cover the common paradigms of various neurodegenerative disorders with their relationship to the immune system. Complexity of the drugs of abuse in this mix will also be covered.

Cytokines

One area where the fields of neuroscience and immunology overlap is the biology of cytokines (Ré and Przedborski 2006). It is essential to expose pre-med students to this vital area of research as a basis for future clinical studies. This is even more important as anti-inflammatory/antiviral cytokines are being used clinically for the management of certain disease conditions.

Cytokines are often termed as chemical messengers that mediate cross talk between cells. They play key roles in orchestrating inflammatory and immune responses. It is the discovery of cytokine signaling between the brain and the immune cells that set a stage for two-way cross talk between the brain and the periphery. It is now widely accepted that not only does systemic infection affect the brain, but, reciprocally, the brain can also influence what happens to the systemic compartment. In this context, the immune system is seen as a sensory organ that not only surveys the outside signals but can also transmit the signals to the brain regarding injury/infection. The brain can then, in turn, set events in motion for the holistic health of the organism. Cytokines play a major role as intercellular messengers connecting these tissues (Rostène et al. 2007). Clinically, advances in this realm have revolutionized our understanding of the disease pathogenesis.

Outcome measures

Students will be evaluated by their participation in the classroom and the quiz offered after each lecture. Major contribution of the grade will also involve clinical/basic presentations made by the students on a specific topic. Students will be judged on their ability to discuss relevant research articles published in peer-reviewed journals. Clinical components will be judged based on the presentation of latest advances in the field. They will also be judged on the clarity of their presentation and their ability to field questions.

Instructional methods

- Didactic lectures – 60%
- Student presentations – 30%
- Special seminars – 10%

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Table 1

NIP course lecture schedule

Lecture No.	Topics
1	Introduction to neuroscience
2	Anatomy and cell types of the CNS
3	Neuronal structure and function
4	Apoptosis/necrosis
5	Th1/Th2 paradigm of cytokine network
6	Seminar: differential expression of cytokines during neuroimmunological disease
7	Signal transduction of cytokine/chemokine/growth factor
8	Blood brain barrier
9	Pathophysiology of neurodegenerative disorders
8	Neuroprotective mechanisms
10	Seminar: how to protect neurons during neuroimmunological disease
11	Immune responses in the CNS
12	Small group discussion of cases including problem solving exercises
13	Interaction of drugs of abuse with the pathological processes in the brain
14	Seminar: using rodent models to examine the bidirectional link between drug abuse and NeuroAIDS