New Developments in Behavioral Pharmacy

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Abstract - Behavioral pharmacology is a scientific discipline that integrates the principles of behavior analysis and general pharmacology. The study of behavioural pharmacology has always been the cornerstone of understanding the processes behind the behaviour of organisms and the biological basis that affect human behaviour, emotions and cognitive impairment. Studies on drug self-administration in humans are reviewed that assessed reinforcing and subjective effects of drugs of abuse. New Insights into Behavioural Pharmacology provides an holistisc view of the present Behavioral Neuropharmacology field. It projects to the future new capabilities that will help researchers to navigate through the complexity of many of todays' neuroscience questions that some years ago seemed technically out of reach. Animals behavior is a powerful tool in Neuroscience but claims of behavior to brain function causality are still often made on the basis of loose associations. In recognition that drug self-administration is but one of many choices available in the lives of humans, the symposium addressed the ways in which choice behavior can be studied in humans. . First, we try to put in context behavioral pharmacology and its relevance and then show some brief examples of how this discipline has developed over the years. Second, we review the concept of a "research model" in preclinical behavioral pharmacology, given the importance of animal models and tests in this area, followed by a brief review of the recent advances using zebra fish as a valuable tool of research. Third, more specific examples are aborded, such as the findings on sleep disorders and those related to sexual hormones and menopause.

Keywords : behavioral pharmacology, psychoactive drugs, behavioral models, psychopharmacology, neuropharmacology, Behavioral medicine

INTRODUCTION –

Every time academics talk about the evolution of human societies and the advance of humanity, language is always mentioned, followed by different pieces of technology that allowed us to change the world. Few times, medicine is mentioned, and within the same area of knowledge, pharmacology is even more frequently omitted. But without the development of pharmacology as a science founded in systematic research, the capacities of medical sciences and therapeutics would be very limited. The goal of this review Human Behavioral Pharmacology is to highlight how research on drug abuse in human behavioral pharmacology has advanced during the last 50 years by utilizing many of the same behavioral approaches in humans as are used in laboratory animal studies. The drug self-administration paradigm has been used for decades to help us understand the variables that may affect drug-taking behavior in the "real world." In doing so, the hope is that this information can be used to develop strategies for reducing drug abuse and its devastating consequences. Most of the active compounds used in medicine were consumed together with the organism which contained them, most frequently plants. As chemistry advanced, scientists succeed in isolating these compounds and described their chemical structure. In consequence, laboratories started to synthesize these Behavioral Pharmacology - From Basic to Clinical Research 2 substances and others with a similar structure that should be tested in research laboratories before using them to treat diseases in humans.

Nowadays, pharmacological research has grown beyond treatments for infectious agents, covering diseases related to the alteration of the normal functioning of the central nervous system (CNS). One of the most important current health problems is related to the addictive behaviors triggered by the consumption of certain substances and the side effects of these addictions: respiratory and cardiovascular diseases in the case of tobacco, metabolic diseases in the case of alcoholism and addictive consumption of refined sugars, infectious diseases in the case of injected drugs, and many others that are not mentioned here. Without losing sight of the fact that addiction is itself a disease of the nervous system with devastating effects per se on the patient's quality of life. In several countries, prescription of different therapeutic agents acting on the CNS to treat psychiatric disorders, such as antidepressants, antipsychotics, and stimulants, has increased. As is true in many areas of behavioral medicine, there is growing interest among pain researchers and clinicians in the role of genetic factors. Diatchenko et al. have proposed a model of chronic pain disorders (e.g., temporandibular joint disorders (TMJD), fibromyalgia, chronic headaches, and chronic pelvic pain) that highlights the role that genetic variability can play in the development of these conditions. The model maintains that the genetic variations, as well as exposure to environmental events, have important effects on two key pathways of vulnerability to chronic pain: psychological distress and enhanced pain sensitivity. In a series of studies conducted mostly on TMJD, Diatchenko, Maixner, and colleagues have demonstrated that: (a) both pain sensitivity and psychological distress are risk factors for the onset and persistence of pain and that genetic variations are linked to pain sensitivity and psychological distress.

In a different perspective, but of a wide interest for behavioral neuroscience, Lopes and Monteiro, introduce readers to the principles and applications of the visual programming language Bonsai (Lopes et al., 2015), an open access tool that permits the simultaneous control of different data streams. They provide the reader with a number of examples and step-by-step tutorials that can be readily implemented by researchers with elementary programming competences. Specifically, when applied to behavioral settings, Bonsai can be used to extract in real time, relevant information regarding animals' behavior (e.g., position, movement, interaction with elements of the setting). More importantly, it can be used to precisely pair electrophysiological information with behavioral readouts.

On the top of that, the system can be programmed to trigger instructions as a function of behavior. In this regard possibilities are immense ranging from the presentation of a cue, delivery of a reward or even optogenetic activation just to name a few. Most of the active compounds used in medicine were consumed together with the organism which contained them, most frequently plants. As chemistry advanced, scientists succeed in isolating these compounds and described their chemical structure. In consequence, laboratories started to synthesize these substances and others with a similar structure that should be tested in research laboratories before using them to treat diseases in humans. In this sense, the development of behavioral pharmacology comprises the development of areas as pharmacology and psychology, experimental analysis of behavior, and recently neuroscience. For a historical review, see [14–16]. However, research in behavioral pharmacology can be summarized in: (1) the development of procedures to screen pharmacological agents for potential clinical effectiveness.

Development of behavioral pharmacology :

Behavioral pharmacology, also known as psychopharmacology, has developed as an interdisciplinary science that comprises fields such as neuroethology, neurochemistry, pharmacology and neuropharmacology, psychophysiology, neurophysiology, experimental analysis of behavior, and several other fields related to neurosciences. Behavioral pharmacology is founded on systematic research with precise methods for assessing and interpreting the effects of chemical, hormones, and drugs on the behavior in humans and experimental animals in order to establish its potential as therapeutic agents or pharmacologic tools to explore how the brain functions and the underlying neurobiological mechanism of cognition, emotions, and behavior. Behavioral pharmacology must thus be an integral component of many neuroscience research programs.

Behavioral pharmacology and sleep disorders :

Pharmacological treatment of sleep disorders is still partially known and not well understood. Currently, extensively pharmacological research is focused in two sleep disorders: insomnia and narcolepsy. Insomnia is defined as the individual's inability to fall asleep, manifested by a long latency to sleep onset and frequent nighttime awakenings experienced three times per week or more, for at least 1 month. Insomnia causes emotional disturbances, impairs cognition, and reduced quality of life. Most epidemiologic studies have found that about one-third of adults (30–36%) report at least one symptom of insomnia, like difficulty initiating sleep or maintaining sleep. Currently, benzodiazepines or Z-drugs (zopiclone, zolpidem, or zaleplon) are the first options to treat insomnia. These drugs act as positive allosteric modulators at the GABAA binding site, potentiating GABAergic inhibitory effects. However, short-term or long-term treatment with these drugs has undesirable effects such as cognitive or memory impairment, the rapid development of tolerance, rebound insomnia upon discontinuation, car accidents or falls, and a substantial risk of abuse and dependence, which make necessary research on new potential therapeutic agents. According to the new evidence-based clinical practice guidelines for the treatment of insomnia, new pharmacology agents for insomnia management are implemented.

Behavioral models of brain disorders :

In behavioral pharmacology, a field that intersects between psychology, neuroscience, and pharmacology [42], different uses are attributed to different epistemic operations and, as a consequence, to different definitions of validity [43, 44]. One of the most basic definitions is that by Paul Willner, which defined screening tests as those uses of animal behavior that are capable of discriminating between different drug effects (i.e., possess high predictive validity); behavioral bioassays as those uses of animal behavior that are capable of shedding light on the neural basis of normal behaviour ; and simulations as those uses of animal behavior that can inform on the etiology, pathophysiology, and treatment of human (mental) disorders. Behavioral bioassays are tests that use nonhuman animals to try to understand the histological, electrophysiological, biochemical, and genetic bases of neurobehavioral functions.

Behavioral pharmacology of steroid hormones in a model of surgical menopause :

Any chapter on behavioral pharmacology would be incomplete without a section reviewing the effects of certain hormones. Behavioral, emotional and affective states are influenced by plasma and brain concentration of steroid hormones in diverse organisms. Particularly, in nonhuman primates and humans there is significant sexual dimorphism respect to behavior and emotional states. Initially, the attributed properties of steroid hormones were related to the maintaining of secondary sexual characters and reproductive function, but some decades ago, it has been established that steroid hormones also influence behavior and some psychiatric disorders. Expression of anxiety- and depression-related behaviors depends on plasma and brain levels of steroid hormones; which in vulnerable subjects could predispose to development of some psychiatric disorder. In humans, anxiety and depression symptoms are more frequent in women than men in a proportion of 3:1. These differences have been attributed to differences in the concentration of steroid hormones. Particularly in women, a high incidence of anxiety and depression symptoms has been identified during physiological states characterized by low concentration of steroid hormones as naturally occur during premenstrual period, post-partum period, and transition to menopause. Preclinical research with laboratory animals has made possible identify the behavioral and emotional changes associated with a reduced concentration of steroid hormones when rats are undergoing to an extirpation of both ovaries which increases vulnerability to stress that can be reverted by injection of severe doses of estradiol.

Behavioral Pharmacology Today :

The current health of behavioral pharmacology is apparent from a brief examination of four aspects of its current status: (a) its place in three major organizations, the American Psychological Association (APA), the Association for Behavior Analysis (ABA), and the American Society for Pharmacology and Experimental Therapeutics (ASPET); (b) its performance within JPET, the pharmacology society's journal; (c) the increasing number of other journals available to authors; and (d) specialty organizations that now serve the field. Association for Behavior Analysis. Although ABA does not have an organized behavioral pharmacology interest group, its

annual convention includes "Behavioral Pharmacology and Toxicology" as a specialty area, with support for invited addresses and guaranteed noncompeting programming. A significant number of interested members attend; the May, 2003, convention devoted about 10 hr to platform presentations and several more hours to about 40 posters. Recent issues of JPET contain more behavioral pharmacology than was the case when psychologists first became involved in the editorial process. From 1966 to 1970, JPET published 1,360 articles, 89 (6.5%) of which contained at least some behavioral research-including measures of analgesia, and so forth. In the single year, 2002, the journal published 578 articles. Of these, 48 (8.3%) were behavioral to some extent. The subgroup of schedule-controlled operant papers also increased as a proportion of all behavioral papers. Between 1966 and 1970, they comprised 2.4% (32 of 1,360) of the total; in 2002, this rose to 3.8% (22 of 578). forth. In the single year, 2002, the journal published 578 articles. Of these, 48 (8.3%) were behavioral to some extent. The subgroup of schedule-controlled operant papers also increased as a proportion of all behavioral papers. Between 1966 and 1970, they comprised 2.4% (32 of 1,360) of the total; in 2002, this rose to 3.8% (22 of 578). on their editorial boards who also publish in JEAB. For BP, 10 of the 24 or so psychologists in editorial positions in 1992, and 10 of the 20 on the 2002 board, have published in JEAB. For ECP, 11 of about 20 psychologists on the initial board in 1993, and 18 of 27 in 2003, have published in JEAB, as have its first two editors: C. R. Schuster and Warren K. Bickel.

Behavioral pharmacology specialty organizations. The number of specialty organizations devoted to behavioral pharmacology continues to grow. The major one for this hemisphere is the Behavioral Pharmacology Society (BPS; founded in 1955). Its annual meetings attract approximately 100 members. BPS has lately been meeting immediately before the annual convention of ASPET, thereby strengthening the latter's new behavioral pharmacology division. There are also the European Behavioural Pharmacology Society (est. 1984; about 320 members) and the Behavioral Toxicology Society (est. 1982; about 50 members). More specialized societies include the Society for Stimulus Properties of Drugs (est. 1978) and the International Study Group Investigating Drugs as Reinforcers (est. 1974), each with about 80 members, as well as the Contingency Management Working Group (est. 1994), whose 40 members study drug abusers.

Unplanned Behavioral Effects :

In many cases, the precise effects that a drug will have in a behavioral preparation are not known in advance of experimentation, but even in cases such as those it is possible on occasion to take advantage of drug-induced behavioral changes to enhance understanding of the behavioral processes involved. A good example of this kind of event is provided in research by Laties (1972). He was studying drug effects on behavior under a fixed-consecutive-number (FCN) procedure. Specifically, pigeons worked in a chamber with two keys, and food reinforcement occurred if the pigeon made eight or more consecutive pecks on one of the two keys before pecking the other. If the pigeon pecked the second key before completing eight or more on the first key, the count reset and the pigeon had to start over. The behavior of pigeons comes under excellent control under such a procedure, with a substantial majority of sequences of pecks on the first key equaling or slightly exceeding eight.

Of theoretical interest is how the pigeon ‘‘does it.’’ That is, there are at least two possible sources of stimulus control that could lead to accurate performance in the task: Switches to the second key could be under the control of the number of pecks just made on the first key (as would be suggested by the way in which the procedure is arranged); it is also possible, however, that because pecks on the first key occur at a fairly constant rate, switches could be under the control of time taken to complete eight pecks. A study of haloperidol by Laties (1972) provided information that helps to distinguish between the two possibilities. Haloperidol had the interesting effect of reducing pecking rate on the first key in a dose-dependent manner. Under nondrug conditions, pigeons pecked the key about 75 times per min.

Under the largest dose of haloperidol, the rate was reduced to about 25 pecks per min. Thus, under this dose of the drug, it took a pigeon about three times as long to finish eight pecks as it had without drug. If switches were under control of the time taken to complete the eight pecks on the first key, then accuracy would be reduced substantially by this dose of the drug. Accuracy, however, was not decreased by this or any other dose of the drug. That finding, coupled with results with other drugs that decreased both rate and accuracy, supports the view that the important controlling variable in the FCN procedure is the response count, not time taken to complete the count. In this case, therefore, Laties was able to take advantage of an unpredicted drug effect to gain information about the sources of behavioral control in a complex behavioral procedure.

Taking advantage of particular drug effects, either planned or unplanned, has occurred less often as a tactic in using drugs to assist in understanding behavior. The approach, nevertheless, has been and presumably can continue to be an effective method in gleaning behavioral significance from drug experiments.

METHODOLOGY-

The first step consisted of a systematic literature review performed. The objective was to assess the terms and definitions that are commonly used to describe Behavirol Pharmacology. Searched Library and PsycINFO from database inception for all papers addressing the taxonomy/terminology used to describe deviations from prescribed drug treatment in ambulatory patients.The main search terms used were ‘Patient compliance’ and ‘Medication adherence’. Because of the problem with translations, the searches were limited to papers in the English language.Detailed search strategies specific to the different databases are provided.

A descriptive synthesis of the extracted data was performed and the historical development of the field was analyzed. Based on the different conceptual approaches identified in the literature review, we derived an initial new taxonomic approach. Conducted a thorough literature search Used various search engines and databases to find relevant articles, books, and other resources related to topic.

This help gather enough information.Human behavioral pharmacology studies recruited via newspapers ads, postings on community bulletin boards, and word of mouth. Clinical populations (e.g., drug abusers, developmentally delayed individuals) are typically recruited from appropriate treatment facilities (e.g., drug abuse treatment clinics). As in any research with humans, protocols must be approved via appropriate institutional review boards and informed consent obtained.

There is no general set of guidelines that must be followed regarding the many ethical issues to be considered when conducting drug studies with humans, but a recent position paper regarding human-subject issues in drug abuse research is worth consulting. A computerized search was performed.

Keywords as "Pharmacology, behaviour pharmacy, Cognitive-Behavioral Interventions, Mild Cognitive Impairments, Elderly People, Interventions, Quality of Life, Caregivers Burden, Positive Participation, Challenging Behaviors, Independence, and behavior" were used to select the studies available in the last decade. A manual search was assessed as completion.

CONCLUSION-

The thesis of this article is that research in behavioral pharmacology has implications not only for issues surrounding behavioral effects of drugs, but it can have significance for the understanding of behavior in general. As mentioned before, behavioral pharmacology is an interdisciplinary field. The present chapter tried to reflect briefly the essence of behavioral pharmacology through an anecdotical review of its developments in areas familiar to the authors. All findings mentioned above underline the importance of the research in behavioral pharmacology on the understanding of the neurobiology of different disorders and the mechanism of action of drugs used to treat such disorders, and at the same time, provide a perspective on the current research done in this growing area, which is and will be a cornerstone in the understanding of human behavior and mental health. Academic pharmacy is now in an excellent position to take the next logical step in its evolution, that is, the full development and incorporation of the behavioral sciences into the professional curriculum. This cannot be accomplished until more attention is given to the severe shortage of appropriately trained faculty with interests in the psychosocial aspects of pharmaceutical care and drug use. Research in behavioral pharmacology has contributed to the study of pharmacological actions of natural products.

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