



PRESIDENT

DAVID GAUVIN, PH.D.

*Drug Enforcement Administration
Drug and Chemical Evaluation
Office of Diversion Control
Washington, D.C. 20537 USA
(202) 353-9585
(202) 307-8570 (FAX)
E-mail: dvgauvin@erols.com*

PRESIDENT-ELECT

MICHAEL SWEDBERG, PH.D.

*Astra-Zeneca Research & Development
General Pharmacology
Forskargatan 20
S-151 85 Södertälje Sweden
46 8553 289 63
46 8553 289 05 (FAX)
E-mail: michael.swedberg@astrazeneca.com*

PAST-PRESIDENT

WOUTER KOEK, PH.D.

*Centre de Recherche Pierre Fabre
17 Avenue Jean Moulin
81106 Castres Cedex France
33 (0) 5 6371 4269
33 (0) 5 6371 4363 (FAX)
E-mail: wkoek@csi.com*

SECRETARY/TREASURER

JENNY WILEY, PH.D.

*Department of Pharmacology &
Toxicology
Virginia Commonwealth University
P.O. Box 980613
410 N. 12th Street
Richmond, VA 23298-0613 USA
(804) 828-2067
(804) 828-2117 (FAX)
E-mail: jwiley@hsc.vcu.edu*

And the next President-Elect is:

It was a close race between Michael Swedberg and Ellen Walker, but all votes are now in. After counting, re-counting, and inventing words like "chad" and "pregnant chad", we now have a new SSPD president-elect. (If you don't understand the joke, ask an American member about our last presidential election!)

Our new president-elect is Michael Swedberg. Congratulations, Michael!

New Members

The Executive Committee would like to welcome our the new members who have joined since the last newsletter was sent:

Anne Jackson, Ph.D. University of Sussex, School of Biological Sciences, Experimental Psychology, Brighton, United Kingdom

Patrik Munzar, M.D. Virginia Commonwealth University, Medical College of Virginia, Department of Pharmacology & Toxicology, Richmond, VA

Michael Nader, Ph.D. Wake Forest University School of Medicine, Department of Physiology & Pharmacology, Winston-Salem, NC

S. Stevens Negus, Ph.D. McLean Hospital, Alcohol and Drug Abuse Research Center, Belmont, MA

Richard Young, Ph.D. Virginia Commonwealth University, School of Pharmacy, Department of Medicinal Chemistry, Richmond, VA

Are you a "Dues Delinquent"?

Have you been meaning to pay your SSPD dues, but have forgotten in the multi-task environment that engulfs us all? It's not too late! Dues for 2001 are now due. The last year that you paid dues is listed on the top right of your mailing label. If the year is not 2001, you have not yet paid dues this year. If the year is 1998 or before, you are in danger of being deleted from our database! If you are still interested in being a member of SSPD, please pay your dues.

SSPD WEBSITE:

<http://www.sspd.org.uk/>

DRUG DISCRIMINATION DATABASE:

<http://www.dd-database.org/>

LETTER FROM THE PRESIDENT

Dear SSPD Members,

It is an unbelievable honor to serve as president of this society in the first year of the millenium. The SSPD was the first professional organization I joined while a graduate student under a future president, Alice Young. It is at every meeting that my commitment to the society is re-affirmed and replenished. This Society has differentiated itself from the myriad of other comparable groupings in it's commitment to remain as it was intended by our founders in the 1970's - an organization of scientists without social barriers or cliques. The student has always been as welcome as the senior researchers who first met in hotel rooms to discuss the issues of the day. Our yearly dues have remained low and our doors remained open because of the continuous friendly atmosphere of some of our most senior past-Presidents such as Don Overton, Jim Appell, and Jim Howard, among others, who are present at almost every meeting. Because of the hard work of the two past presidents, Wouter Koek and Charles France, our society is financially on solid ground. I convey to them our society's full appreciation for all they have done over their years of tenure. It is indeed an honor to stand at the helm of the Society after them. And of course, no president could be fully functional without the competent and motivated endeavors of the Secretary-Treasurer, and it has been our extreme benefit to have Jenny Wiley at the computer and the check book. I, like Jenny, have held that job for two consecutive terms and know the commitment it takes to do the job as well as Jenny has over the last two years. It will also be a distinct privilege to turn all of this over to the incoming-President, Michael Swedberg in 2002.

The Society is sound and growing. We will have two meetings this year. The first meeting will be in Marseilles, France in September the afternoon before the EBBS/EBPS meeting. The second meeting will be held, as usual, in conjunction with the Society for Neuroscience in San Diego, California. The Marseilles meeting will hopefully focus on methodological issues associated with the various stimulus functions of drugs. Wouter has already agreed to discuss statistical limitations of DD research and we are looking for other interested researchers to tackle similar relevant issues. The San Diego meeting will be geared to current research projects and I would encourage student submissions. We welcome the submissions of abstracts for both meetings at any time, and encourage the membership to recruit "new blood" into the Society. I look forward to seeing you all in San Diego or Marseilles.

We would also welcome comments, suggestions, or responses to a submitted proposal to change the by-laws to reflect the two-year tenure of the Presidency of the Society to alternate with the two-year tenure of the Secretary-Treasurer. A number of past-presidents have suggested that these changes would allow for a more effective leadership of the society by stabilizing the executive committee over a longer period of time. A formal vote on this proposal will occur during the October business meeting in San Diego, but I encourage you to let us know your opinions on this specific change to the by-laws.

Yours sincerely,
David Gauvin, Ph.D.
President, SSPD

2001 MEETING NEWS

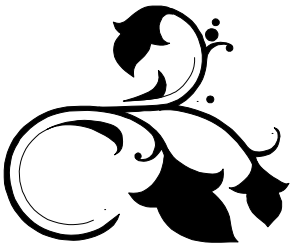
SSPD will sponsor two scientific meetings this year. The first will be held in conjunction with the joint meeting of the European Behavioural Pharmacology Society and European Brain and Behaviour Society (EBPS-EBBS) in Marseilles, France in September. The second meeting will occur in November at the Society for Neuroscience meeting in San Diego, California, U.S.A.

The joint EBPS-EBBS meeting will occur September 8-12. Information on this meeting may be obtained at their website: <http://lncf.cnrs-mrs.fr/EBBS-EBPS-2001/>. SSPD will meet the afternoon of **Saturday, Sept. 8, 1:00 - 5:30 p.m.** The focus of this meeting will be on methodological issues related to the various stimulus properties of drugs, although presentations of results of other research related to the stimulus properties of drugs are also welcome. **Abstracts should be received no later than July 15, 2001.** Please send abstracts to Jenny Wiley (electronic copies appreciated; contact information is on the front page of the newsletter). The opening reception for EBPS-EBBS is scheduled for 6:00 p.m.

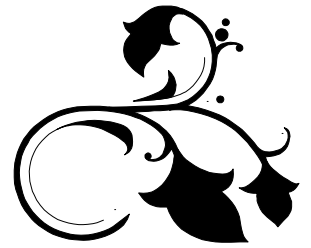
SSPD will sponsor an evening paper session at the Society for Neuroscience meeting that is to be held in San Diego, November 10-15. Information on the SfN meeting may be obtained at their website: <http://www.sfn.org/>. The SSPD session has not yet been scheduled, but, due to restrictions imposed by SfN, it is typically on Tuesday or Wednesday evening. The annual business meeting will be held prior to oral presentations of current research.

For SSPD members who are current on their dues (we thank you), there is no fee for attending the session. (Members who are not current on their dues can pay them at the session.) Non-members will be charged a nominal fee. Food and drink will be provided, and there will be a cash bar for extra drinks.

The deadline for receipt of abstracts is **September 30, 2001**. We particularly encourage students and new members to present their research on the stimulus properties of drugs at this informal forum. The time allotted for each presentation will depend on how many presentations are accepted; in any event, no less than 15 min will be allowed for each speaker. Please send abstracts to Jenny Wiley (electronic format is appreciated). Jenny's contact information is on the first page of the newsletter.



Abstracts of Presentations at the 2000 Annual Meeting in New Orleans



Invited Speakers:

Can drug cues represent a context to which sensitization can be associated? Werner J. Schmidt, Zoologisches Institut, Neuropharmakologie, Universität Tübingen Mohlstr. 54/1, D-72074 Tübingen, Germany.

Behavioural sensitization refers to the intensification of a behaviour upon repeated administration of a drug. Sensitization is nearly inextinguishable and therefore is considered to play a major role in the formation of an "addiction memory". The finding that glutamate/NMDA receptor (R)-antagonists block the development of sensitization has led to the hypothesis that repeated exposure to an addictive drug activates glutamatergic transmission and this promotes drug seeking and relapse. Many findings are in accordance with this view but not all: In several experiments the development of sensitization was not inhibited by NMDA-R-antagonists, however the expression of sensitization (which is tested only under the sensitizing drug) was abolished. This has been explained as a state-dependency effect, i. e. what has been learned in the presence of an NMDA-R-antagonist (here sensitization) can not be expressed in the absence of an NMDA-R-antagonist. State-dependent effects may have been overlooked so far since in many studies animals were treated in the home cages with the sensitizing drug plus the NMDA-R-antagonist and the development of sensitization (for example the day to day increase in locomotion) was not measured in the experimental set up. The state-dependency interpretation was criticised since most of the studies have been conducted with MK-801 and this drug produces sensitization to its own locomotor stimulant effects. To clarify this issue, we chose haloperidol-induced catalepsy (akinesia and rigidity) of the rat that shows pronounced sensitization when repeatedly elicited (known as the "repeated measures effect"). Since acutely administered NMDA-R-antagonists show clear cut anti-cataleptic effects, a possible day to day intensification of catalepsy can not be due to the effects of the NMDA-R-antagonist. We showed that haloperidol-induced catalepsy was counteracted by the NMDA-R-antagonists MK-801, CPPene, eliprodil, Ro 25-6981 as expected, but that the development of sensitization of catalepsy was not inhibited by these drugs. A challenge with haloperidol 14 days after sensitization revealed no sensitized catalepsy, haloperidol plus NMDA-R-antagonist produced the sensitized response and most interestingly, the NMDA-R-antagonist alone also elicited the sensitized response. We concluded from these findings that sensitization of catalepsy developed context dependently i. e. sensitization has been associated to the drug (NMDA-R-antagonist) cue which makes expression of sensitization dependent from the NMDA-R-antagonist state. The paradoxical finding that an anti-cataleptic drug can induce sensitized catalepsy shows that expression of sensitized catalepsy has been rendered completely state-dependent. In conclusion, two forms of sensitization exist, a context-independent (non-associative) form, which can be inhibited by NMDA-R-antagonists, and a context-dependent (associative) form. It may be speculated that in the latter case NMDA-R-antagonists may disrupt the association to the environmental context but instead represent a contextual stimulus to which sensitization can become associated.

Abstracts (cont.)

Drug sensitization, state-dependency and the activation of excitatory amino acid receptors: What are the issues? Paul Vezina, Department of Psychiatry, Committee on Neurobiology, The University of Chicago, Chicago, IL 60637.

Both drug sensitization and state-dependency are well established phenomena that can exert powerful effects on the expression of various behaviors. Recently, a certain degree of controversy has developed over whether the latter phenomenon can provide an alternative account for the apparent ability of glutamate receptor antagonists - dizocilpine, in particular - to prevent the induction of sensitization. In a review of the results from a number of studies, it will first be addressed whether sensitized responding during induction is in fact necessary and sufficient for the subsequent later expression of sensitization. In this context, the actions of the non-competitive NMDA receptor antagonist dizocilpine on behavioral, cellular and biochemical responses during induction and expression of sensitization will be compared to those of competitive antagonists of NMDA as well as non-NMDA receptors and other manipulations impacting excitatory amino acid transmission. While the actions of dizocilpine on acute and sensitized drug-induced responding may be complex, the results of the above experiments taken together strongly support a critical need for excitatory amino acid receptor activation in the induction of drug sensitization. Supported by US PHS grants DA-9397 and DA-9860.

Volunteered presentations:

Tolerance to the midazolam-like discriminative stimulus effects of benzodiazepine agonists in monkeys. Carol A. Paronis, Behavioral Pharmacology Program, McLean Hospital/Harvard Medical School, Belmont, MA 02478

Tolerance to the discriminative stimulus effects of opioids has been well-characterized, however, less is known about the development and expression of tolerance to the discriminative stimulus effects of other drug classes. Moreover, most studies of tolerance to discriminative stimulus effects have used rats as subjects and, to date, there has been only one report that describes tolerance to discriminative stimulus effects in monkeys (Ator and Griffiths, 1993). We investigated the expression of tolerance to the discriminative stimulus effects of benzodiazepines in a group of squirrel monkeys trained to discriminate 0.3 mg/kg midazolam from saline under a schedule of stimulus shock-termination. Because tolerance to the discriminative stimulus effects of opioids is more readily expressed when training is interrupted for the duration of the supplemental administration of the tolerance-inducing drug, initial studies examined the effects of interrupting daily training sessions for six weeks, exposing the animals to intermittent test sessions during this time. Results from these studies demonstrate that the dose-response functions of midazolam, pentobarbital, bretazenil, and zolpidem are not changed during the course of interrupted training sessions. After a period of retraining, daily training sessions were again interrupted and the animals received daily injections of 3 mg/kg diazepam. Starting one week after the beginning of the chronic diazepam regimen, the animals were again tested intermittently. During the course of the daily diazepam exposure, the midazolam dose-effect function was displaced approximately 10-fold to the right and qualitatively similar results were obtained with diazepam, lorazepam, and zolpidem. Following discontinuation of the daily diazepam injections, the dose-effect function of midazolam returned to baseline. These results demonstrate that the interruption of daily training sessions, in and of itself, does not disrupt schedule-controlled performance or alter the discriminative stimulus effects of benzodiazepines in monkeys. However, when the interruption of training sessions is accompanied by daily injections of diazepam, tolerance develops to the discriminative stimulus effects of benzodiazepines. (Supported by PHS grant DA-11453)

Abstracts (cont.)

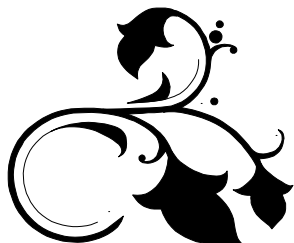
The discriminative stimulus effects of beta adrenergic receptor agonists: an update and concluding remarks. Malath M. Makhay and James M. O'Donnell. Central Michigan University, Dept. of Psychology, Mt. Pleasant, MI 48859.

The discriminative stimulus effects of beta-adrenergic agonists and NE uptake inhibitors have been studied extensively to determine if these drugs are a) centrally active and b) to what extent do these compounds share discriminative stimulus effects. Clenbuterol, a beta-2 adrenergic agonist, has been studied as a discriminative stimulus (McElroy and O'Donnell, 1988; O'Donnell, 1997; Makhay and O'Donnell, 1999) and its stimulus effects are antagonized by the beta adrenergic antagonist, propranolol. Other beta-2 selective agonists such as SOM 1122 and zinterol substitute for clenbuterol as well as the beta-1 adrenergic agonist prenalterol. Dobutamine, a beta-1 selective agonist, partially substitutes for clenbuterol, producing about 75% drug-appropriate responding at the highest dose of 10 mg/kg. It is thought that dobutamine is selective for beta-1 adrenergic receptors, and its selectivity is about 10-fold for beta-1 relative to beta-2 adrenergic receptors (Tuttle and Mills, 1975; Sonnenblick et al., 1979; Platcheka, 1981; Beer et al., 1988; Hays et al., 1985; Ruffolo et al., 1981). Two studies were carried out to examine beta-adrenergic receptor agonist properties. First, a dobutamine-vehicle discrimination was studied. The objectives were 1) to determine if dobutamine can be established as a discriminative stimulus (i.e., centrally active), 2) to characterize the dobutamine stimulus cue, 3) to determine if other direct-acting beta adrenergic agonists, NE uptake inhibitors, and other compounds demonstrating antidepressant-like effects would substitute for the dobutamine stimulus cue and 4) whether down-regulation of beta-2 adrenergic receptors would attenuate the discriminative stimulus effects of dobutamine. Also, the NE uptake inhibitor nisoxetine was examined to determine 1) if a nisoxetine discriminative stimulus cue can be established, 2) if other NE uptake inhibitors substitute for nisoxetine, 3) if it is selective for beta-1 or beta-2 receptors and 4) if beta adrenergic receptor antagonists can block the stimulus cue. Rats were trained to discriminate either 5.6 mg/kg dobutamine from vehicle or 3.2 mg/kg nisoxetine from vehicle. After training, rats were tested with a number of compounds. It was found that clenbuterol, nisoxetine, amitriptyline, protriptyline, maprotiline, and nortriptyline all failed to substitute for the dobutamine stimulus cue. However, imipramine partially substitute for dobutamine at 10 mg/kg. Prenalterol, a purported beta-1 selective adrenergic agonist, completely substituted for dobutamine. Also, rats were given clenbuterol chronically and after 4 days, rats were tested with dobutamine and it was shown that down-regulation of beta-2 receptors did not attenuate dobutamine's discriminative stimulus cue. A dose of 1 mg/kg propranolol reduced drug-appropriate responding to less than 25%. Propranolol and betaxolol (nonselective and beta-1 selective adrenergic antagonists, respectively) failed to antagonize completely the nisoxetine stimulus cue. Clenbuterol failed to substitute for the nisoxetine stimulus cue, but dobutamine substituted completely at the highest dose (18 mg/kg) and desipramine substituted completely for the nisoxetine stimulus cue at the highest dose (10 mg/kg). The inability of full antagonism of the dobutamine stimulus cue and full substitution of clenbuterol suggest that other pharmacological effects of the drug may contribute; this is consistent with the known pharmacology of dobutamine (Ruffolo et al., 1991). The results obtained with the nisoxetine discrimination lead us to conclude that there is beta-1 involvement in nisoxetine's DS effects, but less than complete antagonism might suggest that other actions may contribute to nisoxetine's DS effects.

Abstracts (cont.)

Does route of injection matter in drug discrimination? Robert E. Vann, Scott D. Philibin, Laura E. Wise, and Joseph H. Porter, Department of Psychology, Virginia Commonwealth University, Richmond, Virginia.

The present study examined the importance of injection route for testing drugs in rats trained to discriminate intraperitoneal (IP) injections of 3.0 mg/kg methadone (METH) from vehicle (VEH) in a two-lever drug discrimination procedure. When morphine was injected IP it produced only partial substitution (59.1 %DLR) for METH; however, when morphine was injected subcutaneously (SC), full substitution (89.7 %DLR) was obtained. Similar results were obtained for (+) methadone and (-) methadone. Heroin fully substituted for METH with both IP and SC routes of injection, although the SC route was about 50 times more potent than the IP route. In generalization tests with the training drug METH, the SC route of injection was about 8 times more potent than the IP route was. The kappa agonist U50-488 did not produce METH-appropriate responding with either IP or SC routes of injection. Naltrexone antagonism tests also revealed a similar difference in potency between the IP and SC routes, as a 10-fold increase in the naltrexone dose (given IP) was needed to suppress the discriminative cue of SC METH relative to IP METH. These results demonstrate that the route of injection can play an important role in the results of drug substitution tests in drug discrimination.



Many thanks to all persons who presented papers, participated in discussions, and attended the meeting!

Available Postdoctoral Position

Postdoctoral position available to study the behavioral pharmacology of opioids, benzodiazepines and stimulants in non-humans using drug discrimination, self-administration and other procedures.

Applicant must have a Ph.D. in pharmacology, psychology, neuroscience or other related field. Initial appointment is for one year and is renewable for up to three years. Send CV and the names and addresses of three references to: Charles P. France, Ph.D., Department of Pharmacology, The University of Texas Health Science Center at San Antonio, Mail Code 7764, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900 (e-mail: france@uthscsa.edu).

SSPD Website Update

Thanks to our webmaster, Dominic Stolerman, the SSPD Website continues to be up and running. For the past several months, we have been choosing a published article to highlight on the website. If you have suggestions for future articles that may be of methodological interest to our members, please contact the webmaster.

SSPD would like to express its appreciation to the following companies for their recent generous donations:

Grünenthal
H. Lundbeck A/S
Institut de Recherche Pierre Fabre
Janssen Research Foundation

NOTICE: The next newsletter will be published in late Summer 2001. Ads for positions, comments, articles, etc., should be sent to Jenny Wiley no later than July 15 to ensure inclusion in the Summer newsletter.

Society for Stimulus Properties of Drugs

Jenny Wiley, Ph.D.

Secretary/Treasurer

VCU Box 980613

Richmond, VA 23298-0613