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Upcoming SSPD Meeting

Monday, November 10th (7:30-10:00 p.m.) at the Society for Neuroscience 33rd Annual Meeting, New Orleans November 8 - 12, 2003

<http://www.sfn.org>

SSPD News and Notes

Greetings and welcome to the second installment of the electronic SSPD newsletter. Feel free to forward this newsletter to any colleagues that might be interested in the stimulus properties of drugs. We are also interested in updating our email list of members so forward any new email addresses to Joe Porter. Any items of interest that you have for future newsletters may be submitted to the Secretary/Treasurer Joe Porter (jporter@vcu.edu).

There are a number of SSPD members to thank for their recent and ongoing service to our organization. I would like to take this opportunity to thank outgoing President Michael Swedberg on behalf of the society for his stewardship in 2001-2002. In addition, I would like to thank Ian Stolerman and his son Dominic for the creation and maintenance of our SSPD webpage (<http://www.sspd.org.uk>). Dominic Stolerman, our Webmaster extraordinaire, has handed over his design, construction, and maintenance reins to Adam Prus from Virginia Commonwealth University. Thank you Dominic for the years of service and thank you Adam for taking over this weighty responsibility! Ian has handed over the position of Site Manager to Joe Porter, the Secretary/Treasurer for SSPD. The Site Manager position entails managing the information and membership list that goes onto the website in conjunction with the Webmaster.

A number of previous SSPD members have been surprised to find that SSPD members still gather at Society for Neurosciences each year. I believe this trend in declining attendance reflects two issues. First, most of us interested in the stimulus properties of drugs supplement our research programs with other behavioral and pharmacological assays. Therefore, our SSPD meeting competes with other satellite and ancillary events at the Society for Neurosciences meeting for the attention of our members. For example, in Orlando 2002, our meeting coincided with NIDA's Neurobiology of Relapse satellite meeting. A second issue to consider is that many of our SSPD members only attend Society for Neurosciences meeting every few years. For example, many SSPD members attend the Behavioral Pharmacology/American Society for Pharmacology and Experimental Therapeutics meeting in April. Furthermore, even if these SSPD members that are also BPS/ASPET members do attend Society for Neurosciences, we may lose their company to the popular ASPET social often held on Tuesday nights at SFN! Therefore, we have moved the annual SSPD meeting to **Monday night this year from 7:30–10:00 pm** - room and location of the meeting TBD. If you have any thoughts on these issues, please send your suggestions or comments to me at eawalker@comcast.net.

We hope that the change in meeting time to Monday night in New Orleans will help to draw out our members to hear their colleagues discuss some of the current research underway for the stimulus properties of drugs.

Ellen Walker
President, SSPD

SSPD WEBSITE:

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

DRUG DISCRIMINATION DATABASE:

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

Gift From AstraZeneca

We want to thank **AstraZeneca** (and Past-President Michael Swedberg for his role in obtaining the contribution) for its generous contribution of \$1000.00 to help defray the costs of last year's meeting at Neuroscience.

Call For Abstracts for 2003 SSPD Meeting

If you or your students are interested in presenting a 15-20 min informal paper on your research on the stimulus properties of drugs, please submit an abstract to our Secretary/Treasurer Joe Porter (jporter@vcu.edu) by **October 1, 2003**.

This year a major focus of the oral presentations will be a discussion of drug discrimination methods and some related procedures in mice. However, ALL studies on the stimulus properties of drugs are welcome, so please submit an abstract. We look forward to hearing about your latest research findings!

2002 SSPD Meeting at SFN

Last year, SSPD hosted an evening paper session at the Society for Neuroscience in Orlando, FL on Tuesday night. Thanks to Joe Porter for getting our room and snacks organized on such short notice. Despite conflicting with the NIDA Neurobiology of Relapse satellite meeting, our attendance had tripled from the previous year. Joe was able to collect dues from a number of members, which helped to fill the dwindling coffers. The attending membership at the business meeting suggested moving the meeting earlier in the week for the following year. A lively discussion of the following abstracts ensued. Thank you again to our four speakers (the first authors) for presenting such interesting data on the stimulus properties of drugs.

The abstracts are presented below.

2002 Annual Meeting Abstracts

Discriminative stimulus properties of clozapine: further examination of the role of dopamine, serotonin and cholinergic receptor mechanisms.

¹Adam J. Prus, ²Lisa E. Baker, and ³Herbert Y. Meltzer

¹Virginia Commonwealth University, Richmond, VA

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³Vanderbilt University, Nashville, TN

Clozapine (CLZ) is an atypical antipsychotic which produces minimal extrapyramidal side effects (EPS) and has significant advantages for treating positive symptoms and cognition. The pharmacological actions responsible for these and other advantages of clozapine are believed to involve its actions on dopamine and serotonin receptors, primarily, but there are other candidates, e.g. actions at muscarinic receptors, which have also been implicated. Drug discrimination (DD) studies have been utilized to identify important pharmacological features of clozapine's action. Both low (1.25 mg/kg) and normal (5.0 mg/kg) dose clozapine have been used as training doses in DD studies using rats.

The present study further evaluated the pharmacological basis for the clozapine discriminative stimulus (DS) in rats trained to discriminate either 1.25 mg/kg (N=7) or 5.0 mg/kg (N=7) clozapine from vehicle in a two choice, food reinforced drug discrimination task. The typical antipsychotic haloperidol (0.1-0.4 mg/kg) did not substitute for either CLZ discriminative stimulus (DS), while the atypical antipsychotic melperone (0.37-3.0 mg/kg) engendered full substitution in both groups (> 80% CLZ-appropriate responding). The muscarinic M₁ receptor antagonist trihexyphenidyl engendered full substitution in 1.25 mg/kg CLZ-trained but not 5.0 mg/kg CLZ-trained rats. The 5-HT_{1A} agonist 8-OH-DPAT (0.04-0.16 mg/kg) and the 5-HT_{2A} antagonist M100907 (0.03-1.0 mg/kg) displayed only partial substitution in both groups. 8-OH-DPAT combined with haloperidol did not potentiate drug lever responding greater than 8-OH-DPAT or haloperidol alone. Haloperidol (0.10 mg/kg) and M100907 combinations produced greater CLZ-appropriate responding than either drug alone, but only 1.25 mg/kg subjects (N=2) exhibited greater than 80% CLZ-appropriate responding following 0.1 mg/kg haloperidol + 0.12 mg/kg M100907. Greater stimulus generalization by 5-HT_{2A} and D₂ receptor blockade provides additional evidence that both of these actions, in combination, contribute to the clozapine DS. The present results provide minimal support for the conclusion that a lower training dose (1.25 mg/kg) of CLZ is more useful than a higher dose (5.0 mg/kg) to identify the components of the CLZ DS (Porter et al., 2000).

Influence of Reinforcer Type on the Development and Maintenance of Gamma-Hydroxybutyrate Discrimination in Rats.

Lisa E. Baker, Dori Pynnonen, and Alan D. Poling Western Michigan University, Kalamazoo, MI

Recreational use of gamma-hydroxybutyrate (GHB) appears to be growing in popularity, which is cause for great concern given the recent rise in reported fatalities associated with its use. Unfortunately, relatively little is presently known regarding the neurobehavioral consequences of GHB use. Studies of drugs as discriminative stimuli have played an invaluable role in psychopharmacology. The few studies that have investigated the discriminative stimulus of GHB in nonhumans have reported inconsistent findings, which may be due to a number of important differences in research methodology. As part of an ongoing series of investigations on the discriminative stimulus effects of GHB, the present study investigated possible effects of the type of reinforcer on the development and maintenance of a GHB-vehicle discrimination in rats. Twelve male Sprague-Dawley rats, aged 50-60 days at the beginning of the study, were trained to discriminate GHB (200 mg/kg, IP) from vehicle in a two-choice drug discrimination operant procedure using an FR 20 schedule of food (group 1, n=6) or water (group 2, n=6) reinforcement. Stimulus generalization was assessed with GHB (50-400 mg/kg, IP and IG), the GHB precursor gamma-butyrolactone (GBL, 50-200 mg/kg, IP) and ethanol (1.0-4.0 g/kg, IG). Responding maintained by food was significantly higher than responding maintained by water throughout the duration of the study. Although there was no significant difference between groups with respect to the number of training sessions required to meet the discrimination criterion, terminal accuracy of the discrimination was slightly greater in group 1 than in group 2. GHB produced dose-dependent increases in both groups with full generalization at the training dose following IP administration and at 400 mg/kg when administered orally. GBL produced stimulus generalization in group 2, but only partial generalization in group 1, and substantially disrupted responding in both groups at the highest dose tested. Ethanol (1.0 – 4.0 g/kg) produced only partial generalization in both groups and appeared to disrupt responding to a greater degree in group 2. Results are discussed with respect to potential influences of reinforcer type on response rate and how this might affect GHB-maintained stimulus control.

The discriminative stimulus effects of 5-HT_{2C} compounds in mice.

Ellen Ann Walker, Ph.D.

Department of Psychology, La Salle University, Philadelphia, PA,

Office of Research and Technology Development, Albert Einstein Healthcare Network, Philadelphia, PA

The objectives of this series of experiments were to establish methods for training 5-HT_{2C} compounds as discriminative stimuli in mice. Swiss-Webster and C57Bl/6 mice were trained to discriminate 5-HT_{2C} agonist mCPP using a discriminated conditioned taste aversion (CTA) procedure. On mCPP training days, 4.0 mg/kg mCPP, i.p., was administered 15 min prior to 30-min access to saccharin solution. Mice were then injected with 2.4 mEq/kg LiCl, i.p. On saline training days, saline was injected before and after saccharin access. Swiss-Webster mice learned the discrimination in 6 pairing days. C57Bl/6 mice failed to acquire mCPP as a stimulus. To determine if C57Bl/6 mice are insensitive to the effects of 5-HT_{2C} agonists, mCPP was used to induce CTA. One group of mice received 30-min access to saccharin solution and then 4.0 mg/kg mCPP, i.p. A second group of mice received 30-min access to saccharin solution but then received 32 mg/kg mCPP, i.p. A dose of 32 mg/kg mCPP produced stable CTA whereas 4.0 mg/kg mCPP produced unstable CTA. Another procedure was used to more rapidly establish 5-HT_{2C} compounds as discriminative stimulus in Swiss-Webster mice. A multielement CTA procedure was used to train mice to discriminate between mCPP and saline or mianserin and saline. On the LiCl pairing days, mice were injected with 4.0 mg/kg mCPP or 1.0 mg/kg mianserin i.p. 15 min prior to 30-min access to an almond-scented saccharin solution. Mice then received 2.4 mEq/kg LiCl i.p. On saline pairing days, mice were injected with saline i.p. 15 min prior to 30-min access to a banana-scented NaCl solution. Mice then received saline i.p. Mice rapidly learned the discriminations. To establish the contribution of the training drug, almond scent, and saccharin flavoring to the discrimination, individual elements as well as additional mCPP and mianserin doses were tested alone and in combination. These data indicate that 1) Swiss-Webster mice can learn to discriminate mCPP or mianserin from saline in a pharmacologically relevant manner and 2) C57Bl/6 mice are less sensitive to the effects of mCPP than Swiss-Webster mice. (Supported by USPHS Grant DA 014673).

EFFECTS OF INFUSION RATE ON THE DISCRIMINATIVE EFFECTS OF INTRAVENOUSLY ADMINISTERED MORPHINE IN THE RAT.

M. D. B. Swedberg*, M. Ståhlberg and C. Velasquez.

AstraZeneca R&D Södertälje, Dept. General Pharmacology & Animal Care, S-151 85 Södertälje, Sweden.

The “rush” is an important factor to maintain i.v. drug abuse. It has been assumed that the rush is related to the speed at which a drug is infused intravenously. Indeed, the rate of infusion has been demonstrated to be important to cocaine’s ability to maintain self-administration behavior in monkeys (Balster and Schuster, 1973). It was recently shown that the infusion rate might influence the subjective effects of morphine in human volunteers (Marsch et. al., 2001). The drug discrimination procedure is commonly used to make assumptions about abuse liability in several species. To our knowledge no studies have investigated whether the discriminative effects as the self-administration effects may also depend on the speed at which a drug is administered when given intravenously.

The present study was designed to assess the influence of rate of infusion on the discriminative effects of morphine in rats. Infusions of morphine were administered at two different infusion rates: 2 min or 15 min, respectively, in rats trained to discriminate 10 µmol/kg of subcutaneously administered morphine from no drug. Rats received i.v. infusions via the tail-vein and were then immediately put into the operant test chambers. Doses of 1, 3 or 10 µmol/kg were tested in 8 or 10 rats per dose and infusion condition. The dose response curves did not differ between the two infusion conditions. These data show that the discriminative effects of morphine are not changed between the two infusion rates studied. It is hypothesized that the infusion rates were not sufficiently dissimilar to produce difference in the discriminative effects in the rat.

Balster, R.L. and Shuster, C.R. *J. Exp. Anal. Behav.* 20:119-120, 1973.

Marsch, L. A., Bickel, W. K., Badger, G. J., Rathmell, J., Swedberg, M. D. B., Jonzon, B and Norsten-Höög, C. *J. Pharmacol. Exp. Ther.* 299: 1056-1065, 2001.

Treasurer's Report

As of July 1, 2003 the balance in our checking account is \$3,252.45. A complete report will be presented at the SSPD Business meeting in November.

2004 DUES

Yes – it's that time of year again. I want to thank all of the members who sent in dues payments last year. Most of the membership was one to two years behind in paying dues. As you can see from the checking balance, we need all members to keep up with dues in order to maintain a reasonable balance in our checking account. If you have questions about how much you owe in dues, please contact the Secretary/Treasurer Joe Porter (jporter@vcu.edu).

Please send your check payable to SSPD in the amount of \$20 for your 2004 dues to the Secretary/Treasurer, Joe Porter. If you did not pay your 2003 dues, please make the check out for \$40. If you have been delinquent in your dues for longer than you care to admit – we are offering a one-time special amnesty period – simply pay for 2003 and 2004 (i.e., \$40) and you will be a member in good standing once again. The dues are the primary source of income to pay for the Web Site and the annual meeting so we need all members to stay current in their dues. THANKS!!

WELCOME TO NEW SSPD MEMBERS!

Jolan M. Turner – Graduate Student at University of North Carolina

Steven King – Post Doc at Baylor University

Lawrence Carter – Graduate Student at University of Texas at San Antonio

Ruggero Galici – Faculty at University of Texas at San Antonio

Amy Goodwin – Post Doc at Johns Hopkins University

Eser Ercil – Post Doc at University of Texas at San Antonio

Danielle Paris-Larson – Graduate Student at University of Michigan

Adam Prus – Graduate Student at Virginia Commonwealth University

Alan Pehrson - Graduate Student at Virginia Commonwealth University

Scott Philibin - Graduate Student at Virginia Commonwealth University

PLEASE ENCOURAGE YOUR COLLEAGUES AND GRADUATE STUDENTS TO JOIN SSPD. Contact Joe Porter (jporter@vcu.edu) for information.

Costs of Annual Meeting

Last year's annual meeting was very expensive and the meeting is paid for from the membership dues. Thus, we are looking for ways to increase revenues and/or reduce costs.

One idea is to solicit more support from Pharmaceutical Companies again. A larger balance in the coffers would allow us to gather at other conferences and to cover the increasing costs of these ancillary events. So, if you work for a company that may be interested in supporting our annual meeting or other satellite gatherings please contact our President, Ellen Walker (eawalker@comcast.net).

The second idea for reducing expenses is to have the Society purchase a projector to use at the meetings for PowerPoint presentations. It cost the society \$500 to rent one this past year and a new one can be purchased for \$1000-1100 – thus it would pay for itself in two meetings. Your input on these ideas is needed, so please contact either Ellen (eawalker@comcast.net) or Joe (jporter@vcu.edu) and let us know what you think.
