Effects of REM sleep deprivation on responding under multiple schedules of free-operant avoidance

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The effects of REM sleep deprivation on free-operant avoidance in rats was examined. Six rats were taught to press a lever to postpone shock for a fixed period of time after each response (response-shock [RS] interval). If they failed to press the lever, shocks were delivered after a fixed period of time (shock-shock [SS] interval). The subjects were exposed to a multiple schedule of reinforcement in which RS intervals were varied, but SS intervals were held constant. For each animal, baselines were established in which the length of the RS interval was inversely related to response rate. The subjects were then repeatedly exposed to 24, 48, or 96 h of REM sleep deprivation under identical tank control and cage control conditions. Compared with baseline and control conditions, REM sleep deprivation increased response rates. Increases in response rates were primarily accounted for by increases in brief interresponse times. The percentage of avoided shocks was not significantly altered across conditions.

Operant behavior occurs as a result of an interaction between environmental and biological events (Lubinski & Thompson, 1986). Two primary determinants of operant behavior are positive and negative reinforcement (Catania, 1992). Positive reinforcement occurs when a persistent behavior reliably produces an event. Negative reinforcement occurs when a persistent behavior reliably removes an event or allows it to be avoided. Negative reinforcement typically involves avoidance or escape from noxious stimuli (Hineline, 1981). Examples of negative reinforcement in humans include one's asking a person not to shout when he is talking loudly, the removal of new shoes because they are uncomfortable, or a child's refusal to complete school work (Keller & Schoenfeld, 1950/1995).

Biological events that alter behavior act primarily, although not exclusively, on an organism's central nervous system. Sleep deprivation is one such biological event. For example, the absence of sleep is associated with a wide variety of physiological effects, such as thermoregulatory dysfunction (Shaw, Bergmann, & Rechtschaffen, 1998), alteration in the levels of neurotransmitters such as acetylcholine and serotonin (Jones, 1991), and disruption in synaptic plasticity related to memory consolidation (Smith, 1996). Along with physiological changes, sleep deprivation also alters behavior. For example, it has been shown to increase gross motor

activity in lab animals (Albert, Cicala, & Siegel, 1970), as well as pain sensitivity (Ogilvie & Broughton, 1976) and aggression (Hicks, Moore, Hayes, Phillips, & Hawkins, 1979).

Recently, researchers have demonstrated that increased rates of negatively reinforced aggressive and/or self-destructive behavior in humans is a function of sleep deprivation (R. H. Horner, Day, & Day, 1997; Kennedy & Itkonen, 1993; Kennedy & Meyer, 1996; O'Reilly, 1995). Because of the potential importance of such findings for clinical diagnosis and treatment, the link between negatively reinforced responding and sleep deprivation has been studied using an animal model (Kennedy, Meyer, Werts, & Cushing, 2000). In the Kennedy et al. (2000) study, rats were taught to leverpress in a free-operant avoidance task (i.e., behavior was negatively reinforced). After stable baselines of responding were achieved, the animals were REM sleep deprived for various durations. The Kennedy et al. (2000) results demonstrate that increases in avoidance responding is a function of REM sleep deprivation, relative to baseline or control conditions. Such findings indicate a previously undocumented effect of REM sleep deprivation on behavior that might also be of clinical interest.

The present experiment was designed to further explore the interrelation between REM sleep deprivation and various parameters of free-operant avoidance. The animals were placed on a multiple schedule of free-operant avoidance that varied the magnitude of reinforcement (via response-shock intervals) and response rates of individual animals in the avoidance sessions. The present study was designed to find out what effects various levels of REM sleep deprivation have on operants with differing response rates.

This research was supported in part by funds from the University Research Council and the John F. Kennedy Center's Nicholas Hobbs Society at Vanderbilt University. The author thanks Mark Egli for his software support and Michael Kirby for his laboratory assistance. Correspondence should be addressed to C. H. Kennedy, John F. Kennedy Center, Box 40, Peabody College, Vanderbilt University, Nashville, TN 37203 (e-mail: craig.kennedy@vanderbilt.edu).

Table 1
Sequence of REM Sleep Deprivation (SD),
Tank Control (TC), and Cage Control Conditions (CC)
for Each Animal and Hours of Exposure

Subject					
2	15	18	21	22	25
96CC	96CC	96SD	24CC	24CC	96SD
48SD	48SD	24TC	48CC	48CC	24SD
96SD	24CC	48SD	24SD	96SD	48TC
24TC	48CC	24CC	48SD	24SD	96TC
48SD	48SD	48CC	24SD	48TC	24CC
24CC	24SD	24SD	48TC	96SD	24TC
48CC	48TC	48SD	96TC	48SD	24SD
48SD	96TC	24SD	48SD	24TC	48TC
24SD	48SD	48TC	24TC	96CC	48CC
48TC	24SD	96SD	48TC	96TC	96SD
96TC	24SD	48SD	48CC	48SD	48SD
24CC	96SD	24TC	96SD	24SD	96CC
24SD	96SD	96CC	96SD	96CC	96TC
96SD	24SD	96TC	96CC	48SD	48SD
48TC	48CC	48TC	24CC	24CC	24CC
96CC	24CC	24CC	96CC	48TC	24SD
96TC	96CC	96CC	48SD	24SD	96SD
48CC	96TC	48SD	48SD	24TC	24TC
48SD	24TC	96TC	24SD	24SD	24SD
24SD	96SD	96SD	96SD	48SD	48SD
96SD	24TC	24SD	24TC	96TC	96SD
24SD	48TC	24SD	24SD	96SD	96CC
24TC	96SD	96SD	96SD	96SD	48CC
96SD	48SD	96CC	96TC	48CC	48SD

METHOD

Subjects

The subjects were 6 experimentally naive Sprague-Dawley male rats (numbered 2, 15, 18, 21, 22, and 25). They were individually housed with 24 h ad-lib access to food and water; they weighed between 381 and 466 g at the start of the experiment and were kept on a 12:12-h light:dark cycle with lights on at 6:00 a.m. throughout the study.

Apparatus

BRS/LVE operant conditioning chambers, measuring 31 cm high, 31 cm long, and 26 cm wide, were used. Each chamber was placed in a sound attenuating container with a ventilation fan. Front and back walls were aluminum panels; the sides were made of clear Plexiglas. The instrument panel contained two levers, each placed 2.4 cm from the sides and 3.6 cm from the floor grid. A 28-V houselight was placed at the top and center of the panel. Approximately 0.40 N of downward force actuated either lever. During sessions, 80 dB of white noise was presented via loudspeakers located in the experimental room. A sonalert that produced a 2900-Hz tone at approximately 85 dB was mounted behind the instrument panel of each chamber. The floors consisted of 16 stainless steel rods spaced 1.5 cm apart. A constant-current shock generator and scrambler (MED Associates) was used to deliver a 1-mA shock for 0.5 sec to the floor and instrument panel. The chambers were controlled by MED Associates hardware and by software run on an MMG 386 computer.

REM sleep deprivation was achieved by placing pairs of rats in specially constructed sleep deprivation tanks containing two platforms, each 7 cm in diameter, placed 15 cm apart. The tanks were cylindrical, approximately 1 m high and 0.7 m in diameter. Each rat was seated on a platform, which was raised 1 cm over a depth of 15 cm of water.

Procedure

Initial training. The animals were taught a free-operant avoidance response (Sidman, 1953). The shock-shock (SS) interval

lasted 5 sec. The response-shock (RS) interval lasted 20 sec. The SS interval specified that shocks were to be delivered every 5 sec, unless either the right (for Rats 18 and 22) or the left (for Rats 2, 15, 21, and 25) lever was actuated. Each time the lever was pressed, the RS interval was initiated and shock was postponed for 20 sec. A session began with the onset of houselight illumination, which was maintained for the daily 1 h session. Leverpressing was taught by placing the rat in a chamber for the duration of each session. Daily sessions continued until the animal avoided at least 75% of the programmed shocks per session for 10 consecutive sessions (this took between 10 and 19 sessions).

Multiple avoidance schedule. After initial training, the rats continued to be run in sessions at the same time of day, 7 days per week. However, a schedule of reinforcement different from that in training was used. The new schedule comprised a constant SS interval with alternating RS intervals (see Table 2). A session began with houselight illumination that accompanied the first component (the second component was accompanied by houselight illumination and tone). The first RS interval component was in place for 10 min, followed by a 10-min blackout period (with no shock presented), and then by a 10-min avoidance period with the second RS interval component and another 1-min blackout period. This sequence continued until an animal had been exposed to three repetitions of each RS interval per session. Data from the first two RS components of each session were not used in the data analysis (i.e., these were "warm-up" periods). Data from the other four components were used for data analysis throughout the study.

Once initial baseline stability was achieved (i.e., after 10 consecutive sessions of $\geq 75\%$ avoidance was achieved and response rates appeared stable via visual inspection), the rats were exposed to the REM sleep deprivation, tank control, or cage control conditions (described below). After exposure to an experimental or control condition, each animal was placed in the operant chamber for an avoidance session. Beginning the next day, the animal resumed its daily avoidance regimen and continued until baseline stability was re-established (this took between 3 and 30 days). Each animal was then exposed to another experimental or control condition. This process continued until four exposures to each level of REM sleep deprivation and two exposures to each level of tank control and cage control conditions had occurred for each animal (see Table 1 for each animal's sequence of condition exposures).

REM sleep deprivation. The animals were exposed to 24, 48, or 96 h of REM sleep deprivation via the pedestal-over-water method. This technique eliminates approximately $\geq 98\%$ of REM sleep, but does not affect slow-wave sleep (Maloney, Mainville, & Jones, 1999). Each animal had ad-lib access to food and water while in the tanks.

Tank control. The animals were exposed to tank control conditions for 24, 48, or 96 h. All aspects of the tank control condition were the same as those in the REM sleep deprivation condition, except that the animals were placed on two 16-cm platforms. This condition controlled for possible behavioral effects that might be induced by exposure to the tank environments, but did not restrict sleep (Suchecki & Tufik, 2000).

Cage control. Cage control conditions lasted for 24, 48, or 96 h. In this condition, the animals were kept in their vivarium cage with ad-lib access to food and water. This condition controlled for possible behavioral effects that might be induced by the absence of avoidance sessions.

Results

Response rate. Response rates for each animal are arrayed in Table 2. The table shows the number of responses per minute for each SS and RS interval combination per animal across baseline, REM sleep deprivation, tank control, and cage control conditions. The data for each experimental and control condition and those for each

baseline session that was conducted prior to that condition are summarized in Table 2.

Subjects 2, 18, and 21 demonstrated increased rates of responding only in the 48 h REM sleep deprivation condition, but did not show significant changes in either of the control conditions. Subject 15 demonstrated elevated levels of responding in both the 48- and 96-h REM sleep deprivation conditions, but not in the control conditions. Subject 22 showed increased rates of responding across the 48- and 96-h REM sleep deprivation conditions on the 20-sec RS interval, but not in the control conditions. However, this animal did show increased rates of responding in the 48- and 96-h REM sleep deprivation conditions and in the 96-h cage control condition on the 60-sec RS interval. Finally, Subject 25 showed significant but not systematic changes in response rate as a function of condition type and length of exposure. These differences were confirmed using within-subjects randomized-blocks analyses of variance (RBANOVAs) with post hoc Student's *t* tests set at $p < .05$.

Figure 1 displays the response rate data from Table 2 as the percentage of change for each RS interval in REM sleep deprivation, tank control, and cage control conditions, relative to baseline. The data indicate that the increases in response rates that followed 48 h of REM sleep deprivation were greater for Rats 18, 21, and 22 in the longer RS interval component. Rats 2 and 15 did not show any differential elevations in response rates, and Rat 25 did not evidence any consistent pattern. This pattern of similarities and differences was confirmed using within-subjects RBANOVAs with post hoc Student's *t* tests set at $p < .05$.

Shock avoidance. Table 3 shows the number of shocks avoided per minute by animals across baseline, REM sleep deprivation, tank control, and cage control conditions for each RS interval. The number of shocks delivered was shown to be inversely related to RS interval length for each animal, with longer RS intervals associated with fewer shocks. The pattern for most of the animals indicated no significant difference in the number of shocks avoided across conditions or within RS intervals. Only Subject 25 demonstrated a statistically significant change in avoidance behavior across conditions. The change in avoidance behavior for Subject 25 tended to occur in the REM sleep deprivation and tank control conditions, but this was inconsistent. The data in Table 3 suggest that shock avoidance, except in the case of one animal, was not affected by REM sleep deprivation or control conditions, but was consistently affected by the length of the RS interval. These patterns were confirmed using within-subjects RBANOVAs with post hoc Student's *t* tests set at $p < .05$.

Interresponse time. Given that response rates increased with no change in shock avoidance, a question remains about how REM sleep deprivation changed the pattern of responding that produced these results. Table 4 shows the number of ≤ 5 -sec interresponse times (IRTs)

across conditions for each subject. The data were drawn from the same sessions in Table 3. As is indicated by the information in Table 4, REM sleep deprivation increased brief IRTs (i.e., ≤ 5 sec) for all animals except Subject 25. Within-subjects RBANOVAs demonstrated this difference with post hoc Student's *t* tests at $p < .05$.

DISCUSSION

REM sleep deprivation had several effects on the rats' response rates under multiple schedules of free-operant avoidance. The multiple schedules allowed for the establishment of two different response rates for each animal, permitting an analysis of the rate-dependent effects of REM sleep deprivation. All the animals demonstrated higher response rates and lower shock avoidance under the shorter RS interval schedule. The results demonstrated that 48 h of REM sleep deprivation consistently increased rates of avoidance responding. However, the increases in response rates were not associated with increases in the number of shocks avoided. Perhaps what is most intriguing about these findings is that REM sleep deprivation increased response rates, even though this was not adaptive for the animal in terms of avoiding shock.

Three animals (18, 21, and 22) demonstrated proportionally larger increases in response rates with longer RS intervals (and lower response rates) when they were REM sleep deprived for 48 h. For example, response rates for Rat 18 increased by 77% under an RS 40-sec schedule and by 57% under an RS 10-sec schedule when REM sleep was deprived. However, two other animals (2 and 15) showed proportionally equivalent increases in response rates as a function of 48-h REM sleep deprivation. These data suggest that REM sleep deprivation increases avoidance response rates that have a tendency to produce proportionally larger rate increases for lower response rates (i.e., longer RS intervals).

In the present study, change in response rate was demonstrated to be a function of increased brief (i.e., 5 sec or less) IRTs. Increases in brief IRTs were associated with increases in response rate, but not necessarily with increases in shock avoidance rates. This observation might explain why REM sleep deprivation increased response rates but did not affect shock avoidance rates.

Although not directly analyzed in the present study, it may be of future value to consider the neurobiological mechanisms responsible for the increased response rates. As was noted at the beginning, sleep is a complex neurological process that appears to serve a range of biological and psychological functions. However, researchers interested in understanding the neuropharmacology that underlies behavioral changes caused by REM sleep deprivation might want to consider that reductions in serotonin (5-HT) are a likely mechanism. First, as was also noted at the beginning, REM sleep deprivation has been associated with increases in pain sensitivity, motor ac-

Figure 1. Changes in rate of responding from baseline to REM sleep deprivation, tank control, and cage control conditions for each rat. Data are expressed on the y-axis as percent deviation from baseline response rates. The x-axis arrays information by the number of hours of exposure and the response-shock (RS) interval (in seconds).

Table 2
Mean Avoidance Responses per Minute (With Standard Errors) Across
REM Sleep Deprivation (SD), Tank Control (TC), and Cage Control (CC) Conditions

Subjects	Baseline		24-h CC		24-h TC		24-h SD		48-h CC		48-h TC		48-h SD		96-h CC		96-h TC		96-h SD	
	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE
2 SS = 5																				
RS = 10	6.24	0.12	5.90	0.35	7.50	0.35	7.35	0.48	6.30	0.15	6.75	0.15	9.48	0.49	6.68	0.38	6.63	0.63	7.20	0.08
RS = 20	3.34	0.05	2.78	0.33	3.88	0.93	3.83	0.19	3.48	0.18	3.83	0.18	5.01	0.30	3.45	0	3.58	0.08	3.99	0.25
15 SS = 10																				
RS = 20	6.98	0.17	6.45	0.75	7.70	0.30	6.95	0.88	7.93	0.13	7.85	0.20	10.13	0.66	6.43	0.78	7.53	0.48	10.60	0.24
RS = 40	4.59	0.17	3.90	0.40	4.95	0.10	4.95	0.20	5.10	0.15	4.35	0.30	6.65	0.46	4.75	0.55	5.25	0.10	6.83	0.07
18 SS = 5																				
RS = 10	14.42	0.37	15.38	1.53	15.18	0.13	15.34	0.29	15.33	0.58	14.53	0.23	18.76	0.42	16.68	0.93	17.28	0.83	16.98	1.12
RS = 40	8.15	0.24	8.03	0.68	7.28	2.03	9.00	0.57	9.73	0.18	8.75	1.15	14.33	0.74	10.20	0.85	10.90	1.35	11.94	0.78
21 SS = 10																				
RS = 10	7.54	0.20	6.85	0.05	7.80	0.10	6.90	0.34	7.23	0.98	7.53	0.02	11.06	0.97	8.95	0.15	7.23	1.53	6.79	1.37
RS = 40	4.47	0.18	4.08	0.88	4.55	0.90	3.86	0.59	4.35	0.25	4.35	0.35	7.49	0.47	4.40	0.15	4.68	0.33	4.15	0.77
22 SS = 5																				
RS = 20	4.38	0.06	4.38	0.43	4.45	0.10	4.50	0.19	4.38	0.78	4.70	0.80	5.45	0.13	4.63	0.43	4.60	0.20	5.83	0.78
RS = 60	2.89	0.11	2.15	0.35	3.00	0.20	3.78	0.73	2.83	0.38	3.58	0.53	4.96	0.45	4.35	0.55	2.53	0.23	4.36	0.57
25 SS = 10																				
RS = 10	5.76	0.16	5.85	0.28	4.13	1.03	4.08	0.91	5.65	1.27	5.85	0.40	4.91	0.81	7.50	0.85	4.43	0.63	6.13	0.60
RS = 40	2.92	0.11	3.05	0.30	1.83	0.58	2.40	0.29	2.78	0.08	3.03	0.48	2.78	0.47	3.13	0.18	2.78	0.58	3.06	0.44

Note—SS, shock–shock interval; RS, response–shock interval; intervals measured in seconds.

tivity, and aggression; it is now associated with increased rates of avoidance responding.

Similar behavioral effects have been demonstrated in animals that have received *p*-chlorophenylalanine (PCPA) and 5-HT antagonist injections (Tanaka, Yoh, & Takaori, 1972; Tennen, 1967). Interestingly, these effects have not been achieved when 5-hydroxytryptophan or 5-HT agonists have been administered (Aprison, Hingtgen, & McBride, 1975; Park, Hingtgen, & Aprison, 1991). In addition, the onset of REM sleep has been associated with decreases in 5-HT, particularly in the dorsal raphe

nucleus (L. H. Horner, Sanford, Annis, Pack, & Morrison, 1997; Portas et al., 1998; Portas & McCarley, 1994). It is possible that reductions in 5-HT—due either to REM sleep deprivation or to administration of PCPA or 5-HT antagonists—cause behavioral changes similar to those caused by sleep deprivation because they share a common effect on serotonergic neurotransmission.

In addition to changes in 5-HT levels in the brain, acetylcholine (ACh) activity has also been found to be related to sleep states and their disruption. Jones (1991) noted that ACh activity increased as the sleep state moved

Table 3
Mean Number of Shocks per Minute (With Standard Errors) Across
REM Sleep Deprivation (SD), Tank Control (TC), and Cage Control (CC) Conditions for Each Animal

Subjects	Baseline		24-h CC		24-h TC		24-h SD		48-h CC		48-h TC		48-h SD		96-h CC		96-h TC		96-h SD	
	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE	M	SE
2 SS = 5																				
RS = 10	3.01	0.04	3.25	0.14	2.78	0.01	2.90	0.04	2.94	0.01	2.89	0.01	2.90	0.06	2.93	0.08	3.00	0.07	2.88	0.04
RS = 20	1.60	0.05	1.90	0.34	1.50	0.02	1.50	0.02	1.50	0	1.50	0.02	1.40	0.02	1.60	0.05	1.50	0	1.50	0.07
15 SS = 10																				
RS = 20	0.84	0.09	1.68	0.88	0.53	0.02	1.94	0.36	0.80	0.20	0.68	0.13	0.95	0.19	1.23	0.67	1.26	0.46	1.21	0.13
RS = 40	0.42	0.05	0.55	0.30	0.32	0.02	0.83	0.18	0.35	0.05	0.25	0.16	0.48	0.18	0.53	0.43	0.62	0.07	0.53	0.06
18 SS = 5																				
RS = 10	0.17	0.01	0.11	0.06	0.18	0.04	0.22	0.08	0.20	0.05	0.25	0	0.22	0.02	0.08	0.01	0.08	0.04	0.19	0.05
RS = 40	0.02	0.01	0.02	0	0.04	0.01	0.02	0.01	0.02	0.02	0.01	0.01	0.05	0.04	0.01	0.01	0.01	0.01	0.12	0.05
21 SS = 10																				
RS = 10	2.74	0.24	2.70	0	2.17	0.43	3.46	0.29	3.08	0.53	2.51	0.06	2.23	0.37	2.10	0	3.25	0.62	3.41	0.60
RS = 40	0.48	0.12	0.76	0.36	0.36	0.16	0.73	0.24	0.70	0.05	0.46	0.16	0.50	0.17	0.38	0.08	0.41	0.16	1.01	0.31
22 SS = 5																				
RS = 20	1.12	0.04	1.14	0.17	1.14	0.01	1.12	0.10	1.03	0.31	1.14	0.04	1.06	0.05	1.02	0.14	0.98	0.01	0.95	0.20
RS = 60	0.16	0.01	0.25	0.07	0.11	0.01	0.18	0.05	0.19	0.14	0.17	0.05	0.10	0.02	0.02	0	0.23	0.07	0.23	0.08
25 SS = 10																				
RS = 10	3.11	0.14	3.28	0.62	3.92	0.07	4.48	0.38	3.18	0.04	3.48	0.48	4.06	0.50	1.92	0.02	4.32	0.62	3.62	0.53
RS = 40	0.86	0.07	0.83	0.18	2.17	0.88	1.38	0.36	0.76	0.20	1.45	0.50	1.06	0.29	0.68	0.18	1.32	0.58	1.64	0.72

Note—SS, shock–shock interval; RS, response–shock interval; intervals measured in seconds.

Table 4
Percentage of Interresponse Times That Were ≤ 5 Sec Across
REM Sleep Deprivation (SD), Tank Control (TC), and Cage Control (CC) Conditions

Rats	Baseline	24-h CC	24-h TC	24-h SD	48-h CC	48-h TC	48-h SD	96-h CC	96-h TC	96-h SD
2 (SS = 5)										
RS = 10	57%	53%	64%	60%	59%	55%	79%	57%	51%	63%
RS = 20	59%	62%	43%	55%	59%	61%	81%	60%	63%	58%
15 (SS = 10)										
RS = 20	53%	55%	56%	55%	63%	48%	70%	59%	57%	73%
RS = 40	49%	43%	53%	53%	51%	47%	68%	51%	54%	71%
18 (SS = 5)										
RS = 10	71%	73%	72%	69%	68%	71%	86%	77%	88%	80%
RS = 40	68%	67%	66%	68%	75%	70%	84%	85%	82%	86%
21 (SS = 10)										
RS = 10	61%	64%	62%	58%	60%	62%	82%	74%	57%	61%
RS = 40	65%	63%	65%	63%	67%	66%	85%	69%	61%	65%
22 (SS = 5)										
RS = 20	59%	64%	58%	56%	62%	58%	71%	59%	62%	79%
RS = 60	53%	51%	52%	56%	50%	49%	78%	66%	57%	81%
25 (SS = 10)										
RS = 10	45%	46%	45%	44%	42%	41%	44%	52%	45%	49%
RS = 40	51%	52%	49%	51%	55%	52%	56%	49%	51%	53%

Note—SS, shock–shock interval; RS, response–shock interval; intervals are measured in seconds.

closer to REM sleep and then peaked during this stage. Similarly, Mallick and Thakkar (1992) demonstrated that cholinergic levels, as measured by acetylcholinesterase activity, remained high in rats after deprivation of REM sleep. These findings, along with behavioral evidence for an increase in avoidance responding resulting from exposure to ACh agonists (Balfour, 1990; Hamilton & Grossman, 1969; Ross & Grossman, 1974), suggest a possible role for cholinergic mechanisms involved in the effects of REM sleep deprivation on behavior. However, the viability of the proposed 5-HT and ACh mechanisms and their possible interactions, await further behavioral, neuropharmacological investigation.

Finally, from a clinical perspective, sleep deprivation has been associated with increased aggression and self-injury in people with developmental disabilities (R. H. Horner et al., 1997; Kennedy & Itkonen, 1993; Kennedy & Meyer, 1996; O'Reilly, 1995). In particular, aggression and self-injury function as ways to avoid or escape noxious stimuli—that is, they are negatively reinforced behaviors—and are particularly sensitive to the effects of sleep deprivation. The results of the present study parallel previous clinical findings and provide additional evidence for the role of sleep deprivation in increasing problem behavior. The fact that people with developmental disabilities, including autism and Rett syndrome, experience sleep disorders at a rate much higher than other populations (Brylewski & Wiggs, 1998; Piazza, Fisher, & Kahng, 1996; Quine, 1991) suggests that increased attention should be paid by physicians and psychologists to the comorbidity of sleep problems and problem behavior in this particular population. Whether the previously noted changes in serotonergic and/or cholinergic neurotransmission observed in laboratory settings are func-

tionally involved in human behavioral changes associated with sleep deprivation awaits future analysis.

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(Manuscript received April 19, 2000;
revision accepted for publication July 7, 2000.)