symmetrical about the temporal location of food, with an added positive tail, when plotted against a linear scale of time. The present experiment obtained both the baseline and the symmetry result simultaneously, thus showing that the corresponding argument to a logarithmic, and so to a linear time scale, cannot both be correct.

Gibbon (1981a, 1981b) showed that the baseline result alone is not sufficient to provide a unique scaling of an animal’s time sense because a decision rule must also be involved. Considering linear, logarithmic, or power law possibilities for a time scale and these different similarity rules for the decision process, Gibbon (1981b) was able to reduce the nine resulting possibilities to three on the basis of temporal biastion at the geometric mean. The three surviving models were a difference rule for logarithmic timing and a ratio rule for linear or power law timing. The power law possibility was rejectable on the basis of the frequently observed asymmetrical probability of intermeal time intervals. More recently, Gibbon and Church (1981) have suggested an experiment to test for a between-experimental variable favoring a linear vs. logarithmic time scale. The important point for the present work is that, although temporal biastion at the geometric mean does provide a unique scaling of time, it simultaneously constrains possible models of animal timing.

References

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Selective Adjustment of the Speed of Internal Clock and Memory Processes

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Brown University

Four experiments studied the scaling of time by rats. The purpose was to explore whether animals could be selectively scaled by pharmacological manipulations. All of the experiments used a temporal discrimination procedure in which one response ("short") did not follow another, a second response ("long") was followed by a second food. Each food signal and a different response ("long") was followed by an 8-sec non-reward. Retention of intermeal intervals was also explored. The proportion of "long" responses increased as a function of signal duration. All drugs were administered orthogonally (i.p.) and their effects on the clock memory process was inferred from the observed pattern of change in the point of subjective equality of the psychological functions under testing and testing conditions. Experiment 1 demonstrated that methamphetamine (1.5 mg/kg) could selectively increase clock speed and that haloperidol (1.2 mg/kg) could selectively decrease clock speed. Experiment 2 demonstrated that flupenthixol (0.2 mg/kg) could selectively increase clock speed during continuous administration but leads to a decrease in clock speed below control values when the flupenthixol is discontinued. Experiment 3 demonstrated that valproate (50 mg/kg) rapidly decreases the remembered duration of intermeal times, which suggests that memory storage speed increased. Experiment 4 demonstrated that physostigmine (1.6 mg/kg) can selectively decrease the remembered duration of intermeal times and that acetylcholine (5 mg/kg) can selectively reproduce these remembered durations, which suggests that memory storage speed was differentially affected.

Evidence suggests that animals use at least three distinct stages to process the duration of a signal or of a temporal discrimination task (e.g., Gibbon & Church, in press). The stages are considered distinct to the extent that each can be changed without changing the others. During the first stage (clock stage) objective time is transformed into subjective time (clock readings); during the second stage (memory stage) the clock reading is stored and used during the third stage (decision stage) the clock reading is compared with the memory of the times when reinforcement was given, and a decision is made appropriate for the task. This research is aided, for example, animals respond "long" if the clock reading is greater than some criterion.

Gibbon (1981) described two theoretical representations of animal timing behavior, both of which are derivations of the subjective time in which the clock reading is a power function of objective time. For descriptive purposes this formulation may be multiplied by a constant that is typically set at 1 but is free to vary with changes in clock, memory, or decision stages. A scalar property is assumed such that the slope-adjusted duration of time memory increases with the mean (Gibbon, 1977). In one version of this scalar timing model, variability in temporal discriminations is produced through impre-
citions in the clock stage: an alternative ac-
count for the variability in the memory stage that stores clock readings. In these two cases, the participants were female students and the results are similar, but the interpretation of the parameter values is different. The psychological account is the assumption that processing stages can be dissociated by selec-
tive attention to the effects of a behavior on the stages without affecting the properties of the other stages. The psychological account allows for the possibility that the processing of clock readings can be independent of the processing of memory stages and can be selectively attended to.

Previously, when experimental manipulations produced a change in the way animals scaled time, we have been unable to distinguish between explanations involving a change in the clock stage and changes in the way animals scaled time. In the present study, we have manipulated the correspondence between objective time, clock time, and subjective time. These manipulations will be represented differentially by animals that have acquired a discrimination between the two conditions. The clock stage and memory stage will be differentially attended by animals that have acquired the discrimination under normal conditions following the manipulation.

The difference is illustrated by a comparison of the behavior of animals that have been trained in a discrimination between a particular drug that affects the timing of a drug that affects the time of a drug and a drug that affects the timing of a drug that affects the time of a drug. In one condition, a drug that affects the timing of a drug that affects the time of a drug is administered in the presence of a drug that affects the timing of a drug that affects the time of a drug. In the other condition, a drug that affects the timing of a drug that affects the time of a drug is administered in the presence of a drug that affects the timing of a drug that affects the time of a drug. The difference is illustrated by a comparison of the behavior of animals that have been trained in a discrimination between a particular drug that affects the timing of a drug that affects the time of a drug and a drug that affects the timing of a drug that affects the time of a drug. In one condition, a drug that affects the timing of a drug that affects the time of a drug is administered in the presence of a drug that affects the timing of a drug that affects the time of a drug. In the other condition, a drug that affects the timing of a drug that affects the time of a drug is administered in the presence of a drug that affects the timing of a drug that affects the time of a drug.

Once the experiments were set up, we found that the animals that received the drug that affects the timing of a drug that affects the time of a drug exhibited a change in the way they scaled time. In the other condition, the animals that received the drug that affects the timing of a drug that affects the time of a drug exhibited a change in the way they scaled time. The difference is illustrated by a comparison of the behavior of animals that have been trained in a discrimination between a particular drug that affects the timing of a drug that affects the time of a drug and a drug that affects the timing of a drug that affects the time of a drug. In one condition, a drug that affects the timing of a drug that affects the time of a drug is administered in the presence of a drug that affects the timing of a drug that affects the time of a drug. In the other condition, a drug that affects the timing of a drug that affects the time of a drug is administered in the presence of a drug that affects the timing of a drug that affects the time of a drug.

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Table 1: Experimental Design

<table>
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<tr>
<th>Condition</th>
<th>Experimental</th>
<th>Control</th>
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<tr>
<td>A</td>
<td>Train + drug</td>
<td>Train + water</td>
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<tr>
<td>B</td>
<td>Train + drug</td>
<td>Train + water</td>
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<td>C</td>
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Note: There were five subjects in each group.

- Oxygen uptake of equal numbers of drug and saline injected rats was measured using an open-circuit respirometer to evaluate the effect of the drug on cardiac output and ventilation. The effects of the drug on cardiac output and ventilation were not determined in the current study.

- The results of the experiment were analyzed using a two-way ANOVA (factor 1: drug treatment; factor 2: saline treatment). The main effects of drug treatment and saline treatment were significant, and there was a significant interaction between the two factors. The post-hoc analysis using the Tukey-Kramer test revealed that the drug treatment significantly increased oxygen uptake compared to the saline treatment.

- The data were presented as mean ± standard error (SE), and the statistical significance was set at p < 0.05. The study was approved by the institutional animal care and use committee.

Experiment 1: The Effect of Meperidine on Heart Rate and Blood Pressure

- The effects of meperidine on heart rate and blood pressure were measured in rats treated with a single intramuscular injection of meperidine (10 mg/kg) and controls treated with saline. The heart rate and blood pressure were measured over a period of 60 minutes after the injection.

- The results showed that meperidine increased heart rate and blood pressure significantly compared to the saline controls. The heart rate increased by 25% and the blood pressure increased by 30% in the meperidine-treated group compared to the saline-treated group.

- The data were analyzed using a two-way ANOVA (factor 1: drug treatment; factor 2: time). The main effects of drug treatment and time were significant, and there was a significant interaction between the two factors. The post-hoc analysis using the Tukey-Kramer test revealed that the drug treatment significantly increased heart rate and blood pressure compared to the saline treatment.

- The data were presented as mean ± standard error (SE), and the statistical significance was set at p < 0.05. The study was approved by the institutional animal care and use committee.
rescued by the animal in accordance with the following equations: \( t = \frac{K}{T + M} = \frac{T}{K + T} \), where \( K \) = clock constant and \( T \) = memory constant. Normal clock and memory constants are given a relative value of 1 and any increase or decrease is expressed as a proportion of this normal value. In the case in which the clock reading is selectively increased, \( t > M > K \), because \( K > 1 \) and \( T = 1 \). If animals are later tested under conditions in which the clock constant is returned to normal \( K = 1 \), then \( t > T \) the relation between \( T \) and \( W \) will be left unaffected, at least initially, because a change in \( M \) requires new learning. The result of this selective change in the relation of \( t \) to \( T \) following training is a rightward shift in the psychophysical function and higher PSE. A similar result, but with a leftward shift in the psychophysical function and a lower PSE, would occur if animals, previously trained with a decreased clock constant \( K < 1 \), then \( t > T \), were returned to normal conditions (\( K = 1 \), thus \( t = T \)) during test sessions.

**Methods**

Procedure: After pretreatment (see General Method section) training and testing with methamphetamine and haloperidol begun.

- Ethanol-conditioned rats were trained under ethanol-methamphetamine (0.1 mg/kg) and then tested following saline injections in ethanol-paired days. The results obtained from these rats were compared to 15 control rats trained under saline and the paired following methamphetamine injections on paired ethanol days.

- Animals 13 experimental rats were trained under haloperidol and then tested following haloperidol injections in ethanol-paired days. Three groups of three rats were compared to another 13 control rats trained under saline and then tested following haloperidol injections on ethanol-paired days.

- Drugs: Methamphetamine and haloperidol (Haldol) were given up to 0.9 mg/kg i.p. 20 min prior to food-restricted training; methamphetamine volume was 2.5 ml in all cases.

**Results**

Two-signal training. A proportion-correct measure was calculated by dividing the total number of correct responses by the total number of signals. Because correction trial data was included in this measure, the proportion correct was free to vary from 0% to 100%. During the 9 days of two-signal training there were no reliable differences in the proportion-correct measure between the 2- and 8-signal acquisition for any group, \( n(14) < 1 \).

Figure 1 shows the mean proportion correct for each condition as a function of sessions compared by first averaging over 2- and 8-signal duration and then taking a median across animals. The smooth curve near the data points is derived from the theory described in the General Discussion section. For each treatment the \( p \)-portion of "long".

**Figure 2.** Median proportion of "long." responses as a function of signal duration during the last three sessions of seven-signal training (left panel) and testing (right panel). Open circles indicate experimental rats trained under haloperidol (METH) and tested under saline, closed triangles indicate control rats trained under saline and tested under METH. The data points are derived from the theory described in the General Discussion section.

The smooth curve near the data points is derived from the theory described in the General Discussion section. For each treatment the \( p \)-portion of "long."
administered ip 20 min before a 3 h ses-
tion) and tested under a saline-prob-
cue procedure had a light-induced shift of the psycho-
physical function during saline probe ses-
sions. The interaction of the administration of haloperidol led to a de-
crease in clock speed and a corresponding decrease in the PSE on the saline side of the skew, but not on the control side. This could be due to the stimulation of the dopamine system by the haloperidol or a result of the saline condition. If methamphetamine increases clock speed, it would be expected that the function relating latency to signal duration would be upward. Both shifts were ob-
served.

In summary, the major conclusion from the pattern of the PSE changes in the psychophysical functions relating the latency and the number of "long" responses to signal duration was that drugs known to increase the dopamine system and modify central nervous system functions, in part through their effect on dopamine neurons (e.g., Iversen & Iversen, 1981; McGee, Eccles, & McGee, 1970), have been shown to selectively affect the clock stage (e.g., K) while not changing the mem-
ory stage (e.g., J).

Gibson and Church (in press) described a model in more detail what the control condition was consistent of. In their information-processing model of timing, a pacemaker with a periodically repeated pulse with an interpulse interval, \( r = \tau ^{+} \), where \( \tau \) is the rate of pulse generation, and these pulses are "switched" into an accumula-
tor. The accumulator simply sums the number of pulses that are applied to it, and the value stored in the accumulator as a function of signal duration serves as the clock reading. This reading is linear with physical time if the rate of the pulse generation is constant. The proposal made here is that the effective level of brain dopamine sets the rate of pulse generation for the clock stage.

Experiment 2: The Effect of Footshock Stress on the Internal Clock

The behavioral, neurological, and electrophysiological similarities of amphet-
amines and stress have been well documented (e.g., Antman, 1975, 1978; Schi-
er, Black, & Kochan, 1980; Udvin, Kvet-
nam, & Kojar, 1976). An experimental similarity is that both amphetamine and stress increase the effective level of dopamine, and they can affect certain be-
haviors (e.g., locomotion, stereotypy, and-

cession) in a manner that is often indivi-
distinguishable (Antman et al., 1983). The pres-
t experiment examined the possibility that the use of continuous footshock stress would be similar to methamphetamine in its ability to selectively increase the rate of an internal clock.

In addition, this experiment explored the possibility that the biochemical mecha-
nisms involved in time perception might be similar to those involved in the use of continuous footshock stress (i.e., exposed rats trained without the stress).

Figure 5. Mean percentage correct as a function of sessions during continuous footshock (open circle indicates without continuous foot-
shock stress) and closed circles indicate control (rats trained without the stress).
The main conclusion was that low levels of continuous feedback lead to increased performance, while higher levels of feedback have a detrimental effect on performance. Further analysis revealed that the optimal level of feedback was approximately 50% of the total response time.
whose components are designed to be mutually regulating such that any change in activity in one component (e.g., increase in clock speed) will be counterbalanced by a concomitant change in the activity of another component. When such a system is in operation it will reduce the magnitude of any initial deflection even while the input is still present. The observation that the leftward shift of the psychophysical function produced by the continuous footshock stress. during testing was greater during the first half of the session than during the second half, although the stimulation remained constant, supports this claim. The opponent process, however, is postulated to be sluggish in its latency, recruitment, and decay and will be most evident when the stimulating stimulus is suddenly terminated. The persistence of the opponent process will be seen for some time, perhaps hours, because of this sluggish decay property (e.g., Antinman, 1975, Solomon & Corbit, 1974). The observation of a decrease in clock speed behind control values during the last of the punishment steps is consistent with this argument. To date, the notion of reciprocally antagonistic processes in systems has fared well in accounting for the mechanisms of various drug interactions (e.g., McGregor, Grewal, & McGregor, 1974) and time-dependent variations in avertly motivated behaviors (e.g., Antinman, 1975). It is argued that neurochemical changes produced by footshock stress, the role of serotonin as the opponent to dopamine action has been postulated by Dyste (e.g., Cushing, 1981; Gallop, 1981; Harvey & Deakin, 1981). It is clear that either an opponent association is hypothesized or for determining clock speed and variability, but the opponent process model of time perception seems worth emphasizing.

Experiment 1: The Effect of Vaepoeris and Oxytocin on Memory Processes

Experiments 1 and 2 demonstrated that the clock stage could be changed independently of the memory stage used in timing tasks. The present experiment investigated whether the neuropeptides vasopressin and oxytocin differentially affect the acquisition and steady-state performance of a temporal discrimination in a manner consistent with a selective change in the memory stage. Vasopressin has been implicated in learning and memory processes because it facilitates the acquisition, consolidation, and retrieval of information in animals and humans (e.g., de Wied & Bouls, 1980; Javitt & Krupanskj, 1977; McCrenor & McGee, 1980; Weller, Huffman, Gwilliam, Lantos, & Fecter, 1980; Heijs et al., 1981; Witter & de Wied, 1980). Each of these cognitive changes is uncertain. One proposal is that vasopressin derivatives speed up consolidation and memory maturation processes, thereby making them more efficient and increasing accessibility to new change structures necessary for information processing (e.g., Rager, van Rijmen, de Wied, 1974; De Wever et al., 1981; Witter & de Wied, 1980). Oxytocin, a related neuropeptide, is also believed to affect learning and memory, but in an opposite manner to vasopressin facilitates consolidation and retrieval as measured in a passive-avoidance task, whereas oxytocin attenuates these effects (e.g., Kowak, Bouls, & Vestenberg, 1976; Ko- vaks, Bouls, Vestenberg, de Koker, & de Wind, 1976; Witter & de Wied, 1980)

When animals are trained under normal (saline control) conditions, the clock reading (T) directly reflects objective time (T, c) and reference memory (M) accurately scores (N - I, M) of the conditioned to be used for memory comparisons. Under these conditions, both the clock constant (K) and the memory constant (P) are equal to I. It is in this way, that the psychophysical functions for animals trained under normal conditions is close to the mean equal to the mean psychophysical mean of the two refined physical conditions and the value of the clock reference measurement (I - I) or 4 sec., as measured and in the psychophysical function. In addition to the above, subjects were trained under normal conditions in which the release of the relaxation of the clock reading was gradual and the clock constant (K) remained unchanged (K = I). In this case, the relation of M to T will gradually change increasing over time, because the relaxation of the clock constant (K) remains unchanged. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. The results obtained from these animals were compared to control rats trained under saline and then trained following repeated saline injections on selected probe days. When animals are trained under condi-
Seven-signal training. The median performance of the rats during each squad's last three sessions of seven-signal training is shown by the psychophysical functions in the left panels of Figures 10 (vasopressin) and 11 (oxytocin). Figure 10 (left panel) shows the data from the three signal ranges for rats trained under vasopressin or saline plotted on a proportional time axis and scaled in values appropriate to each range. When scaled in these ways, the psychophysical functions for the saline-controlled conditions under the three different ranges of signal durations are similar. The same is true for animals trained under vasopressin. This proportionality result supports Weber's law. Figure 11 (left panel) shows the performance of rats trained under either oxytocin or saline. For each treatment the proportion of "long" responses increased as a function of signal duration, but the PSFs differed. The PSF for rats trained under vasopressin was 1.84 sec (for the 1-4 range), 3.68 sec (for the 2-4 range), and 7.26 sec (for the 4-16 range). For rats trained under saline the PSFs were 2.06 sec (for the 1-4 range), 4.03 sec (for the 2-4 range), and 8.06 sec (for the 4-16 range). The PSFs of rats trained under saline were close to the geometric mean between the two extreme signals (2.0, 4.0, and 8.0 sec). In contrast, the PSFs of rats trained under vasopressin were reduced by approxi- mately 10% compared to rats trained under saline. The DLs for the three groups trained under vasopressin were 33, 67, and 1.28 sec, respectively. The Weber fraction was constant at .18. The DLs for the three groups trained under saline were 45, 85, and 1.71 sec, respectively. The Weber fraction was nearly constant (.22, .21, and .21). The best fitting theoretical functions for the 2-4 second vasopressin and saline-training conditions differed significantly between the two treatments in fitting individuals from each condition, P(4) > .31, P < .01. Training at the 2-8 range under oxytocin produced a PSF of 3.7 sec for rats trained under saline. The PSE was 4.02 sec. The DL for rats trained under oxytocin was 40 sec and the Weber fraction was .31; for rats trained under saline the DL was 56 sec and the Weber fraction was .14. The best fitting theoretical functions differed significantly between the two training conditions, P(4) > .38, P < .01.

Testing. The median performance of the rats during the three test sessions is shown in the right panels of Figure 10 and 11. For each treatment the proportion of "long" responses again increased as a function of signal duration. The PSE was 3.68 sec for rats trained under vasopressin and tested under saline. 4.02 sec for rats trained under saline and tested under vasopressin, 3.67 sec for rats trained under oxytocin and tested under saline, and 4.03 sec for rats trained under saline and tested under oxytocin. The DLs for the four groups were 7.7, 70, 40, and 43 sec, respectively. The Weber fractions were .18, .17, .11, and .11, respectively. The leftward shift in the psychophysical functions observed during training under vasopressin and oxytocin persisted when these same rats were tested under saline. There was no change in the PSE for rats trained under saline and tested under vasopressin or oxytocin; thus the major difference between experimental and control groups continued during testing. P(4) < .31, P < .01. With additional test days, the functions adjusted such that rats trained under saline had a median PSE not reliably different from 4 sec, and rats tested under vasopressin or oxytocin had a PSE reliably less than 4 sec.

The relation between median response latency and signal duration is shown in Figure 11 for training under vasopressin, oxytocin, and saline-control conditions in the 2-8 range. The response-latency functions for the other signal ranges were not reliably different in any of the measures presented. The median proportion of the responses excluded from this analysis by the 3-sec latency cutoff was 12% ± 2% for the vasopressin and oxytocin conditions and 23% ± 1% for the saline-control conditions. There was a significantly higher percentage of responses with latency less than or equal to 3 sec under drug conditions than under saline conditions, P(28) > .39, P < .01. The median response latency was 93 sec for rats tested under vasopressin, 95 sec for rats tested under oxytocin, and 130 sec for rats trained under saline. There was a nonsignificant difference between drug treatments, P(28) < .1, and a significant difference between drug and saline conditions, P(28) > .24, P < .01. The latency of 12 of 15 rats trained under vasopressin (binominal test, p < .05) and 13 of 15 rats trained under oxytocin (binominal test, p < .05) was longer than the middle (4 sec) signal duration than at either extreme duration (2 or 8 sec), and the latency was shorter for the shortest signal duration.
Figure 12. Mean response latency as a function of sig- nal duration during the last three training or testing ses- sions for rats in the 2-sec range. (Closed circles indicate sessions at water deprivation; open circles signify sessions at ad lib feeding; closed diamonds signify those during which the water-deprived rats were trained under saline; open diamonds are those in which water-deprived rats were trained under saline).

duration than for the longest one in 21 of 30 cases (binomial test, p < 0.05). The latency of 23 of 23 rats trained under saline conditions was longer at the 5-sec signal duration than at any other extreme duration (binomial test, p < 0.01), and the latency was shorter for the short- est signal duration than for the longest one in 24 of 30 cases (binomial test, p < 0.01). Finally, the signal duration with the mean response latency was significantly lower for drugs than for saline conditions, 4.75 ± 2.91, p < 0.01.

Discussion

There were five major effects of vasopres- sin (0.07 pressor units/kg administered in 20 min, before a 3-hr session) and oxytocin (0.02 pressor units/kg administered in 20 min, before a 3-hr session) on the psychophysical time-discrimination function.

The number of trials required to reach asymptotic performance was significantly reduced by vasopressin and oxytocin. This is interpreted as an increase in the rate of learn- ing because the drugs increased the rate-of- acquisition parameter but not the asymptotic parameter for the linear operator model. How the drugs facilitated learning is unclear. Perhaps the drugs produced a peripheral sensory effect that caused the auditory stimuli to become more "salient." Alternatively, the linear rate of acquisition may be related to an increase in the memory constant, a greater sensitivity to trials, or a reduction in required latency. Any of these effects might be expected to facilitate learning.

The shift in the PSE produced by both vasoprespin and oxytocin was in the direction and on the same order of magnitude as that produced by testing with 5.5 cycles of methamphetamine in Experiment 1, but the two effects appeared to be fundamentally different. The leftward shift of the psycho- physical functions continued during training, while the chronic administration of vasoprespin or oxytocin but not under chronic admin- istration of methamphetamine. The lack of a receding effect was interpreted as a decrease in the memory of reinforced trials, which may have developed as an increase in clock speed. The assumption is that vasoprespin and oxytocin produced an increase in the memory constant (T > 1), thereby causing memory to misrepresent a clock reading that directly reflected objective time (M = T / T - 1).

The termination of chronic vasoprespin and oxytocin did not produce a rightward shift of the psychophysical functions as did the termination of chronic methamphet- amine. Instead, the leftward shift not observed during training was maintained throughout testing. This result indicates a rela- tively permanent effect produced by the drugs that is consistent with a change in memory whereby the animal enters this test stage with an underestimate of the memory constant (T) that was acquired from an initial clock functioning at normal speed. The difference lines of the psychophysical functions was significantly reduced by both vasoprespin and oxytocin. This is consistent with the few instances in which a drug facilitated the discriminative performance of animals (e.g., Blough, 1957; Leaton & Kendrick, 1972; Wahrton, 1972). Such a result does not appear to be directly related to the question of whether the clock constant or memory constant can be selectively changed but is related to the question of whether the vari- ability of these processes can be adjusted (see General Discussion section).

Vasoprespin and oxytocin significantly re- duced the response latency to all signal dura- tions and produced a leftward shift in the maximum of this function. Short-latency re- sponders have been found to be more accurate than the average of all responders (Marquis & Church, 1983; Marqui, et al., 1981). The latency reduction produced by vasoprespin and oxytocin may not in itself account for the lower DL of these same psychophysical func- tions, because additional analysis revealed that other decreases in the latency cutoff did not lower the DL for control or experi- mental groups, and so latency cutoffs were different (e.g., 1.5 sec) the DL was usually increased.

In general, the results do not support prev- ous studies in which different effects of vasoprespin and oxytocin were observed (e.g., Kovacs, et al., 1979). Intraventricular admin- istration of these drugs may produce different results from intraperitoneal administration (see Werd, 1976) and high doses of oxytocin can mimic the effects of vasoprespin (Witter & De Werd, 1980). It is unlikely, however, that these explanations are applicable to all stud- ies because low doses are commonly used and intrapituitary administrations of vasoprespin and oxytocin have previously produced differential effects. One possible explanation for the observed discrepancy is that the major support for differential effects comes from a comparison of the behavior obtained follow- ing the first administration of the two drugs. The data from a number of studies indicate that a significant difference between vasopres- spin and oxytocin exists only during the first day of administration. Performance for animals receiving vasoprespin was signifi- cantly better than it was for saline-control groups, and performance for animals receiv- ing oxytocin was significantly worse than it was for saline-control groups. The difference between the two drug treatments diminished following the first administration (e.g., Witter & De Werd, 1980). This finding suggests that oxytocin may reverse some detrimental side effects in addition to the facilitating effects and that the animal may become tolerant to these side effects following the initial admin- istration. In the present study rats received their first drug injection prior to their fourth pretrial session; hence the probability of observing any drug-induced side effects dur- ing training was reduced.

As described earlier, the clock process might consist of a pacemaker, switch, and accumulator, collectively called the "internal clock." Given this design, longer signal du- rations would lead to greater accumulations (clock readings) that might require more time to be stored in reference memory than would the accumulations produced by shorter signal durations because there is a larger quantity to transfer. If clock readings are viewed as concrete quantities distributed in an anatomical space, it might be reasonable to assume that longer clock readings will require more storage time for incorporation into ref- erence memory than will shorter clock read- ings (e.g., Thatcher & John, 1977). The spe- cific proposal is that M = T / T - 1, or at another way, M = accumulation or spatial distribu- tion (speed of memory storage). Given an ac- cumulation, memory might estimate or represent its value according to the amount of time required to process it. If this theory were true, there would be an inverse relation between mem- ory storage speed (process) and the remem- bered duration of a physical stimulus (content).

In addition, it might be that the faster a clock reading is stored, the less variability will enter into the process. This would in- crease sensitivity to time. The slower a clock reading is stored, the more variability might enter into the process. This would decrease sensitivity to time. It is uncertain what would contribute to the variability; perhaps the clock reading is susceptible to decay (clock retesting).

In summary, the results indicate that both vasoprespin and oxytocin decrease the re- membered value of reinforced durations in a proportional manner that is consistent with an increase in the memory constant (T) and is inconsistent with a change in the clock con- stant (K). The current interpretation of this result is that these drugs selectively increased memory storage speed; thereby the remem- bered times of reinforcement are proportion- ally decreased. These procedures may have resulted in a greater amount of memory stor-
age of retinal cells because more neurons were involved or because the speed of chemical processes, mediating memory storage, were accelerated (Johnson, 1967). The drug-produced improvement in the DL is consistent with this memory-storage-speed hypothesis and is in agreement with previous findings that alterations of certain neurophysi-sides of neurophysiological origin facilitate learning and memory processes (e.g., de Wied, 1974; van Winsum & Grosshans, Bohus, & de Wied, 1981).

Experiment 4: The Effect of Phystostigmine and Atropine on Memory Processes

Do drugs that differentially interact with central cholinergic systems, such as physostigmine and atropine, differentially affect the speed of memory storage processes in a temporal discrimination task? This experiment was similar to Experiment 3; its purpose was to determine if memory representations for different memory durations could be transferred to lower or higher values without producing a corre-

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Figure 12. Median proportion correct on a function of stimulus duration in Experiment 1. The median proportion correct for each condition is produced in a function of stimulus duration. The PSE (see General Method section) for rats trained under atropine was 3.67 sec, for rats trained under atropine with saline was 4.45 sec, and for rats trained under saline (averaged over both saline groups) was 4.93 sec. DAs for the three groups were 35, 1.31, and 45 sec, respectively. The set of model parameters used to fit the psychophysical function was reliably different from the set of model parameters used to fit the median proportion correct function in calibrating the individuals from

The median rate of acquisition was $r = .02$ for rats trained under physostigmine, $r = .04$ for rats trained under saline, and $r = .22$ for rats trained under atropine. Phystostig-

Figure 14. Median proportion of "long" responses in a function of signal duration during the last three signal presentations (left panel) and testing (right panel). Open circles indicate experimental rats trained under physostigmine (PBS) and atropine and closed circles indicate control rats trained under saline and PBS.
and for a longer signal duration under atropine than under saline in 15 of 15 cases for each treatment (bisomial test, p < .01).

Discussion

The psychophysical functions obtained for training under physostigmine and atropine were different from functions obtained under normal training conditions (e.g., Church & Delay, 1977) and for training under methamphetamine and haloperidol (Experiment 1). That is, the point of subjective equality was significantly less than (physostigmine) or greater than (atropine) the geometric mean of the two reinforced physical durations. Training under chronic physostigmine (0.1 mg/kg administered ip 20 min. before a 3-hr. session) produced a permanent leftward shift and a 49% decrease in the difference of the psychophysical function relating the probability of a "long" response to signal duration. Church, Chertkow, and Olenko (in press) demonstrated that in a modified Batchelor procedure (peak procedure) a flunitrazepam-induced decrease in the shift of the Gaussian response function relating response probability to signal duration. The leftward shift produced by the lesion was interpreted as a decrease in the remembered time of reinforcement, possibly due to an increase in the effective level of acetylcholine.

If a rat was always trained after physostigmine administration, the PSE on both a subjective and objective time scale would be lower if memory storage speed were increased (M = 1/7X). By reference memory consistently "mimicking" the clock, rats would be unable to adjust their temporal criterion, and the times of reinforcement would be consistently underestimated, as observed. Rats that were trained under chronic physostigmine were then tested under saline-control conditions. The memory storage speed intertemporal function is that, under saline testing conditions, reference memory would be storing accumulated signal values at its normal speed, but as noted previously, responding would be initially determined by the originally acquired memory values, and no shift in the PSE of the psychophysical function should occur, as observed. Rats trained under saline conditions and tested under physostigmine showed a decrease in the DL, but no shift in the PSE.

Thus, the data are consistent with the effect that an increase in memory storage speed would have if remembered values of times of reinforcement directly reflected objective time and were consistent with a change in clock speed. Taken together, the data suggest that physostigmine increases the speed of memory storage processes, thereby changing the correspondence between clock speed and not affecting the speed of the internal clock.

Training under chronic atropine (0.05 mg/kg administered in 20 min. before a 3-hr. session) produced a permanent rightward shift and an increase in the difference times of the psychophysical function relating the probability of a "long" response to signal duration. Maricq (Note 2) demonstrated that a lesion of the medial frontal cortex of rats produced a permanent rightward shift, with no change in the difference times of the psychophysical function relating probability of a "long" response to signal duration. This permanent rightward shift in the PSE, produced by the lesion, can be interpreted as an increase in the remembered times of reinforcement.
which is possibly the result of a decrease in the effective level of acetylcholine.

If a rat was always trained after atropine administration, the PSE as both the subjective and objective time scale would be higher if memory storage time were decreased (M = 17.1). By memory consistently "misreading" the clock, rats would be unable to adjust their criterion and the times of reinforcement should be consistently overestimated.

Rats trained under chronic atropine were tested under saline-controlled conditions. The memory storage time interval as a result of atropine is that under saline testing, memory will be storing accumulated values following which a response is reinforced at its normal speed, and responding will be initially determined by the originally acquired memory values and level shift in the PSE of the psychophysical function should occur, as observed. Rats trained under saline conditions and tested under atropine showed a decrease in the delay, no shift in the PSE, which was consistent with the experiment that a change in memory storage speed would have if remembered times of reinforcement are divided by the subjective rate and inconsistent with a change in clock speed. Taken together, the data suggest that atropine decreases the speed of memory storage processes, thereby changing the correspondence between clock memory and while actually responding the speed of the internal clock.

An analysis of response latency and performance of signal duration showed that the signal duration from the start of the response latency to the latency during training was decreased by pharmacological and increased by atropine. A possible explanation of this change is that relative latency is inversely related to the expectation of reinforcement of a response following a particular presentation. A decrease in the subjective rate of signal duration implies that subjective proportionally decreases the remembered durations of reinforced times. It would be expected to shift the function relating response latency to signal duration leftward. If atropine proportionally increases the remembered durations of reinforced times, it would be expected to shift the function relating response latency to signal duration rightward.

In summary, the major conclusion from the pattern of the PSE changes in the psychophysical functions relating the proportion of "long" responses to signal duration is that drugs known to cross the blood-brain barrier and modify central nervous system functions, in part through their action on cholinergic neurons (e.g., tetrabenazine, 1961; MacGnall et al., 1978, 1983) tend to affect the memory storage (e.g., Y) while not changing the clock speed directly (e.g., K).

The results suggest that photomotor-accelerates and increases discrete memory storage speed. Thus, in the former case rats remembered their clock readings as being shorter than they actually were, in the latter case rats remembered that clock readings as being longer than they actually were.

General Discussion

The speed of a rat's internal clock is selectively adjusted. Some manipulations that increase the effective level of dopamine increase clock speed (e.g., methamphetamine) or decrease continuous feeding (e.g., amphetamine) that decrease the effective level of dopamine decreases clock speed (e.g., haloperidol and removal of continuous food reinforcement). Increasing the speed of the internal clock proportionally increases subjective times.

Opponent processes in clock speed can be observed under appropriate conditions. This finding suggests that the processes are involved in the nicotine and nicotine response latency is inversely related to the expectation of reinforcement of a response following a particular presentation. One way, this occurs is if the clock speed is closer to the mean subjective rate of reinforcement of the left response, it makes a right response if the clock speed is closer to the mean subjective rate of reinforcement of the right response. On any given trial, the animal makes the correct response if the clock speed is closer to the mean subjective rate of reinforcement of the left response and reinforces a right response if the clock speed is closer to the mean subjective rate of reinforcement of the right response. The measure of distance a is a ratio between clock time and memory time, as described below.

A Scalar Timing Model

A schematic representation of the central features of the timing process that underlies the theoretical curves in the figure is shown in Figure 17. It is assumed that internal cues are available that can be interpreted over time. This is a "clock" that can be run, recharged, or reset.

partionally decrease the values of remembered durations.

There is some relation between drugs that affect memory storage speed and the accuracy of time discriminations. Drugs that increase memory storage speed increase accuracy, and drugs that decrease memory storage speed decrease accuracy. A change in sensitivity to time as measured by the DL of the subject can be observed, however, prior to any observed change in the reference memory for the interval times as measured by the PSE. This dissociation between the DL and the PSE remains to be explained.

The precise form of the psychophysical function provides evidence for the discrimination processes involved. The point of subjective equality of the temporal discrimination function is typically near the geometric mean of the reinforced times and equipment, and the Weber fraction is fairly constant over a wide range of signal durations (Church & Deluty, 1977; Stedile, 1983) Gibbons developed several models of time discrimination for visual stimuli. It is suggested that the curve plotted on the right includes a number of subjective time points that are corresponding to the subjective times observed. The lower the ratio, the more sensitive the animal is to time. As $x_2$ is $\mu_2$, this becomes an increasingly accurate estimate of $T$.

When the signal duration is a, a left response is reinforced. The main subjective time of reinforcement is $\mu_2$ and we assume that this value is remembered accurately. A similar argument, when the signal duration is $a$, a right response is reinforced, the main subjective time of reinforcement is $\mu_1$, and we assume that this value is remembered exactly.

On a give trial in which the signal duration is $a$, the subjective time $g = a T$. The animal compares the distance of the current subjective time to the remembered time of reinforcement of the short response $\mu_1$ and the remembered time of reinforcement of the long response $\mu_2$, and responds to the closer one. The specific rule is as follows: Response "long" if $a \mu_1 > a \mu_2$, and "short" if $a \mu_1 < a \mu_2$. This indifference is predicted by the geometric model of C and L. This process may be modeled or calculated with the equations derived by Gibbons.
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(1971, Equation 17). The special case of the

3. $P(T, S, S) = 4|v(T - S)|$ (17)

4. $P(T, S, S) = 4|v(T - S)|$ (17)

5. The mean clock speed at the time of an

6. $K = Y$ (17)

7. Although $K$ and $Y$ would normally be

8. free to vary simultaneously, the sake of

9. simplicity, the current application of the

10. model was effective in these studies.

11. Psychophysical functions were fit, allowing

12. only $K$ and $Y$ to vary for any one experimen-

tal manipulation while the other three

13. parameters were free to vary at all times.

14. The mean for this selective variable is

15. $K$ and $Y$ are not distinguishable by the form

16. of the psychophysical function but only by

17. whether the leftward or rightward shift in the

18. function is permanent or not. A horizontal

19. shift maintained by drug administration is

20. interpreted as a change in $K$, and a tempora-

21. ry shift is interpreted as a change in $K$.

22. Subjects may not always attend to the sig-

23. nal duration. On such trials, the proc-

24. ed by the above equation cannot apply. It

25. is assumed that any very particular trial of

26. the animal is attending to the signal duration

27. with some probability, $p(t)$, and inter-stimuli

28. is modeled by the process described above;

29. however, with probability $1 - p(t)$, the ani-

30. mal is not attending to the signal duration, and

31. on these trials its probability of respond-

32. ing "long" ("L") is some constant bias, $p(L|T) = a$.

33. The term $p(t)$ is called "atten-

34. tion," and $p(L|T - a)$ is called "response-

35. ness" or the probability of a "long" response

36. given attention (cf. Church & Gilford, 1981). The

37. fitting procedure used an exhaustive search of

38. the parameter space (with a step size of 0.05). Categorization (fast memory storage speed vs.

39. slow memory storage speed) were specified by the parameter values that provided the optimal fit to the differen-

40. t patterns of group response functions. Statisti-

41. cal analysis determined which categora-

42. tical parameter best fit the data. The results are

43. displayed in Table 2. The overall square

44. rotated values in accordance with. Note that in all cases the variance accounted for is 99% or better. Thus, at a descriptive level, the

45. theory is relatively good at characterizing behav-

46. ior. Much better fits could be obtained, e.g., 99.9% of the variance ac-

47. counted for with less systematic deviations if the step size were reduced, but greater gener-

48. alizability of parameter when across conditions and experiments was obtained by using the 0.5 step size. The PSE estimates of differences between treatments were based on the relatively large step size used, and similar con-

49. clusions are reached if PSE and DL measures are obtained from a linear regression analysis such as that used by MacLennan et al., 1981.

50. The purpose of this investigation was to demon-

51. strate that internal clock and objective processes are separable empirically. This was done by selectively adjusting the speed of

52. these processes. There are of course other ways to change the relation between clock reading and objective time without affecting the

53. spurious trend in reference memory. The in-

54. ternal clock could be temporarily stopped during the timed signal. This would lead to a rightward shift of the response function (e.g., Meck et al., in press). Alternatively, the concord of reference memory could be changed without affecting the functioning of the internal clock by shifting reinforcement to another duration on the stimulus contin-

55. um. Neither of these manipulations appear to involve a fundamental change in the way objective time is gauged. At present only phar-

56. macological manipulations of the effects can be produced to such a scaling change.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Procedure</th>
<th>Procedure</th>
<th>Procedure</th>
<th>Procedure</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Y$</td>
<td>$K$</td>
<td>$p(T)$</td>
<td>$p(S)$</td>
<td>$p(L)$</td>
<td>$DL$</td>
</tr>
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<td>1</td>
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<td>4.03</td>
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<tr>
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<tr>
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<td>Mix-Test</td>
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<td>1</td>
<td>995</td>
<td>3.66</td>
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<tr>
<td>4</td>
<td>Mix-Test</td>
<td>1</td>
<td>1</td>
<td>995</td>
<td>3.66</td>
</tr>
</tbody>
</table>

NOTE: PSE = point of subjective equality; DL = difference limit; Wt = Weber fraction.
Table 3
Descriptive Summary of Results

<table>
<thead>
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<th>Empirical</th>
<th>Formal</th>
<th>Psychological</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>4</td>
<td>DA</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Note: In increase in; * = increase in. ACh = acetylcholine; DA = dopamine; PSE = point of subjective equality.

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psychologically (e.g., increase in clock speed), and (d) physiologically (e.g., increase in effective level of dopamine). The value of y that was used most frequently (3.3) is similar to that previously observed as an optimal fit for temporal discriminations; the same is true for the value of p(4)(1, 0.0; e.g., Meck & Church, in press-a, press-b).

We therefore concluded that methamphetamine increases the probability of a "long" response to signal duration when administered to rats trained under salicylic acid and produces a rightward shift when training under chronic methamphetamine is terminated. This change in behavior was fit by changing only the K parameter of the scalar timing model, suggesting an interpretation of the effect of methamphetamine as being due to an increase in clock speed. Experiment 1 also demonstrated that a discrete procedural shift in the psychophysical function can affect the relative likelihood of a "long" response to signal duration when administered to rats trained under salicylic acid and produces a leftward shift when training under chronic haloperidol is terminated. This change in behavior was also fit by changing only the K parameter of the model, but the direction of the change had the opposite effect on the interpretation of the effect of haloperidol as being due to a decreasing rate of dopamine. It appears that the effects of both methamphetamine and haloperidol suggest that the effective level of dopamine is a major determinant in setting clock speed in the rat.

Experiment 2 demonstrated that continuous footshock stress produces a significant increase in the difference limen. It also produces a leftward shift in the psychophysical function relating the probability of a "long" response to signal duration when administered to rats trained under salicylic acid and produces a rightward shift when training under chronic continuous footshock stress is terminated. These changes in behavior were fit by changing y and K in the model, although p(4) also changed somewhat. This led to an interpretation of the effects of footshock stress as being due to a decrease in sensitivity to time caused by an increase in the variability of the clock and an increase in clock speed. Experiment 2 also demonstrated that the termination of continuous footshock stress on tests for subjects that had been trained under salicylic acid leads to a rightward shift in the psychophysical function. This shift was fit by a change in K and is interpreted as a decrease in clock speed that acts as an opponent to the increase in clock speed produced by the continuous administration of footshock stress. The results for continuous footshock stress also support the suggestion that the effective level of dopamine sets clock speed because footshock stress increases the release of dopamine in the brain.

Experiment 3 demonstrated that vasopressin and oxytocin decrease the difference limen of the psychophysical function and the probability of a "long" response to signal duration when administered during test days rats trained under salicylic acid. These drugs also produce a decrease in the difference limen and a permanent leftward shift in the psychophysical function when chronically administered. The changes in the difference limen were fit by changing y, and the leftward shift was fit by an increase in y, which led to an interpretation of the effects of vasopressin and oxytocin as being due to an increase in sensitivity to time caused by a decrease in the variability of the clock and an increase in memory storage speed. The relation of the effects of these neurohormones to a particular neurotransmitter or physiological mechanism is uncertain, but Meck (Note 1) proposed that the effects of these hormones are mediated, in part, by cholinergic systems.

Experiment 4 demonstrated that physiostigmine decreases the difference limen of the psychophysical function relating the probability of a "long" response to signal duration when administered during test days to rats trained under salicylic acid and a decrease in the difference limen and a permanent leftward shift when chronically administered. The decrease in the difference limen was fit by a decrease in y, and the leftward shift was fit by an increase in x, which led to an interpretation of the effects of physostigmine as being due to an increase in sensitivity to time caused by a decrease in the variability of the clock and an increase in memory storage speed. Experiment 4 also demonstrated that atropine produces an increase in the difference limen of the psychophysical function relating the probability of a "long" response to signal duration when administered during test days to rats trained under salicylic acid and an increase in the difference limen and a permanent rightward shift when chronically administered. The increase in the difference limen was fit by an increase in y, and the rightward shift was fit by a decrease in the y parameter of the scalar timing model, which led to an interpretation of the effects of atropine as being due to a decrease in sensitivity to time caused by an increase in the variability of the clock and a decrease in memory storage speed. Taken together, the effects of both physostigmine and atropine suggest that the effective level of acetylcholine is a major determinant in setting memory storage speed in the rat.

There is no claim that the drugs used in this study exclusively affect processes related to time discrimination. The fact that some of the results could be interpreted in terms of one or two of these pharmacological mechanisms shows that these training procedures can isolate the timing system from other behavioral systems (e.g., locomotion and motivational systems). The conclusions reached in each of the experiments must be limited by the absence of a dose-response relationship. It is not assumed that the results obtained by using a single dose of a particular drug are necessarily generalizable to other doses of the same drug. The main point is that pharmacological agents can be successfully used as tools to study cognitive processes of animals.

References

References
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