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Time Structure Analysis of Behavioral Acts Using a Computer Pattern Recognition System

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KERNAN, W. J., JR., P. J. MULLENIX AND D. L. HOPPER. *Time structure analysis of behavioral acts using a computer pattern recognition system.* PHARMACOL BIOCHEM BEHAV **34**(4) 863–869, 1989.—The spontaneous behavior of rats was monitored, classified and analyzed using a recently developed computer pattern recognition system. The K-function, a parameter developed for statistical research on spatial point processes and patterns, is used to analyze the temporal structure of behavioral acts or the joint relationship of separate acts. Forty male rats were observed in two experiments. In Experiment 1 untreated rats were observed and the temporal structure of their behavior was analyzed to establish an estimate of the false-positive error rate appropriate for use in such analyses. In Experiment 2, 20 control rats and 20 rats exposed to 2.0 mg/kg d-amphetamine were monitored using the computer pattern recognition system. The data from Experiment 1 showed that the false-positive rate was approximately ten percent or less. Experiment 2 demonstrated that the temporal structure of spontaneous motor behavior of amphetamine-treated rats was significantly disrupted.

Behavior K-function Rat Amphetamine Pattern recognition

DIRECT observation is one of the oldest methods of obtaining information on a phenomenon of interest. This methodology has found extensive use in the behavioral sciences (13); however, the time consuming nature of direct observation and the limitations of the human observer have, until recently, restricted its usefulness. The advent of modern computer image analysis equipment and software has allowed the development of a computer based pattern recognition system capable of classifying the spontaneous behavioral acts of the laboratory rat (7). In addition to automating the observation of behavior, this system permits the collection and analysis of a multitude of dependent measures, i.e., initiations, durations and temporal structure.

The temporal relationships of the initiations of the various acts constitute a source of information on the structure of behavior and upon changes induced by exposure to various agents. Previously available analytical methods have been of limited success in studying time structure data (8). To improve such analyses, a technique for analyzing spatial point processes and patterns was applied to the analysis of the temporal structure of behavior (8,10).

In the development of the time structure analysis, the behavioral data analyzed came from the same set of experiments involving a human observer and time-lapse photography (9, 11, 12). The observational environment was identical for all of these experiments. It consisted of a Plexiglas box divided into two chambers. One chamber contained a control rat and the other contained a treated rat. As the rats explored this novel environment, their activity was recorded for fifteen minutes using time-lapse photography at one frame per second. Using a list of

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TABLE 1

THE BEHAVIORAL TAXONOMY FOR THE RAPID SYSTEM

	RAPID System	
	Act	Group
Major Body Position	Stand	Attention
	Sit	Grooming
	Rear	Explore
	Walk	Explore
	Lying down	Grooming
Modifiers	Blank	Attention
	Grooming	Grooming
	Looking	Attention
	Sniffing	Explore
	Washing face	Grooming
	Smelling	Attention
	Head turning	Attention
	Turning	Explore

operationally defined acts, trained human observers would subsequently record the activity occurring for each rat in each frame. In addition to analyzing separate acts, certain of these acts, which are related by function and share a similar time structure, were combined, for analysis, into groups (8). Throughout the present paper these groups of acts will be referred to as "group acts" and this term should not be confused with treatment groups. With these human-scored data, the false-positive rate found for group acts was approximately 2% in data sets specifically constructed so that behavioral changes were not expected (8). In addition, for the analysis of data sets where behavioral effects were expected (induced by phenytoin and nitrous oxide), the rate of positive signals rose to approximately 30%. Using the same data and techniques, but a more extensive list of acts, the false-positive rate was approximately 5% and the observed positive signals in the phenytoin and nitrous oxide experiments remained in the range of 20 to 40% (10).

Recently, a new system was designed to perform similar behavioral studies, but in a more automated fashion (7). For convenience this new computer pattern recognition system is given the acronym RAPID (Rat Activity Pattern Identification Device). In the conversion from time-lapse photography and a human observer to the RAPID system, certain systematic differences occurred. First, the RAPID system could classify and record most, but not all, of the behavioral acts identified by a human observer in time-lapse photographic studies. The behaviors bobbing, scratching and pawing were eliminated from the RAPID taxonomy (Table 1) because of the faster scan time of video cameras versus the slower shutter speed used in the time-lapse studies (7). In that these three behaviors occur only infrequently in time-lapse data, their loss is insignificant with respect to time structure analyses using RAPID. Second, RAPID classifies the behavioral acts walking, turning and head turning with greater precision and consistency than a human observer. It is more precise because the two camera views eliminated the directional dependence innate to the one camera view of the time-lapse photographic method. The two camera views with RAPID allow accurate measurement of the center-of-mass of the animal, the angle of orientation of the body and the angle from the center-of-mass to the nose of the animal. Comparisons of these values between sequential frames by the computer prevent the common human error of substituting more readily identifiable modifiers like looking, sniffing and smelling for the movements turning and head turning. Third, RAPID does not identify as well as a human observer the acts grooming, washing face and, to a lesser extent sniffing.

When changes in the classification are known to occur, either as a result of improvements, a loss of classification accuracy, or some mixture of both, changes in the false-positive rate in the analysis of time structure of behavioral acts in control experiments are expected. Even if all of the changes are improvements, there is no a priori method of determining whether this rate will decrease, increase or be unaffected. The relationship between the measures of time structure and the initiations of the acts is too complicated to analytically predict from prior data what the false-positive rates will be for RAPID.

The purpose of this study is to evaluate the capabilities of the new RAPID system by estimating false-positive rates and evaluating the changes in the time structure that are associated with amphetamine exposure. To examine these questions, two experiments were performed. In Experiment 1, the "control experiment," untreated male rats were tested to establish false-positive error rates. In Experiment 2, one of each pair of rats was given d-amphetamine to alter its behavior and to test how well behavioral changes are detected using the RAPID system and K-function calculations.

METHOD

Eighty pathogen-free Sprague-Dawley male rats (250 g) were obtained from Charles River and housed in the Forsyth animal facility. They were housed two per cage (7″ × 7″ × 10″), and they were given Purina Rat Chow (5012) and water ad lib. Their light cycle was maintained on a 12 hour light (0600–1800 hr)/12 hour dark period.

The rats were tested in a novel environment separate from the animal quarters. For the Experiment 1, twenty pairs of rats were left untreated. For the Experiment 2 another forty rats were randomly selected; twenty were injected (SC) with 2.0 mg/kg d-amphetamine sulfate and paired with another twenty injected with an equal volume of normal saline. Thirty minutes after injection, the animals were placed in the observation chamber and testing began. All behavioral tests were conducted during the diurnal period between 0900 and 1300 hr each day. Following the behavioral tests, all animals were euthanatized using pentobarbital sodium.

Details of the test environment, the test procedure and the RAPID system have been previously described (7). The test in the RAPID system consisted of placing a pair of rats simultaneously into a Plexiglas box. The pair was separated by a clear partition with small holes, which allowed the animals to see and smell each other while they explored the novel environment for 15 minutes. Two video cameras taking a frame per second were used to monitor their spontaneous behavior. The video signals were transferred to a Micro VAX I and VAX 11/750 for pattern analysis and behavioral classification of the data.

The behaviors classified by RAPID are listed in Table 1. Each specific act identified by the computer (7) is listed along with its corresponding group act that has been previously described (8). The shorter, group act taxonomy was developed when it was found that the major body positions and modifiers belonged to three groups, where the components in each group were preferentially linked in time (14). These groups were arbitrarily labelled "grooming," "exploratory" and "attention." A body position may correspond to one of these three groups, for example walk is an exploratory act, and the modifier which is co-occurring with this body position may correspond to a different group, for example head-turning is an attention act. The act walk head-turn would then be labelled "explore/attention." The other two possible combi-

nations among the original three groups would include "attention/groom" and "explore/groom." These six categories constitute the list of group acts used in this study.

For purposes of data analysis, the false-positive rate and changes induced by amphetamine were determined for both the full list of acts and the group acts. Also for purposes of data analysis, determination of the false-positive rate in the Experiment 1 was accomplished by alternately labelling the rats as "control" and "exposed" even though all of these rats were untreated.

Data Analysis

Calculation of time distribution and time sequence. In analogy with the statistical research devoted to the analysis of spatial point patterns (2, 15, 16) a function which can be used to study the time structure of the initiations of the behavioral act α was defined (8) as:

$$K_\alpha(t) = \frac{\tau_\alpha}{(N_\alpha^2)}\left[\sum_{i\neq}\sum_{j} W_{ij}^{-1} I_t(U_{ij}^{\alpha})\right] \quad (1)$$

In this equation N_α is the number of initiations of act α, τ_α is the total observational time corrected for the extension of act α, W_{ij} is an edge correction term, and $I_t(U_{ij}^{\alpha})$ is 1 (or 0) depending upon whether the pair (i,j) of initiations of act α occur (do not occur) within a time separation t. We refer to $K_\alpha(t)$ as the time distribution of act α.

The definition of $K_\alpha(t)$ was constructed so as to minimize the effect of changes in the average number of initiations of α and changes in the average duration of this act. The use of a corrected observational time arises from this effort. If the animal begins act α and this act continues through m successive observations, the next initiation of act α cannot possibly occur until a different act is initiated. If the total time of observation is T, the number of α initiations is N_α and the total time observed for act α is t_α, the corrected observational time to be used for this act is:

$$\tau_\alpha = (T - t_\alpha) + N_\alpha \quad (2)$$

Throughout this paper "time" is treated as a mathematically discrete variable and N_α is present in Eq. (2) so that the time of initiation is included in the count for the corrected time.

When act α occurs near the beginning or end of the observation period, the W_{ij} edge correction factor must be applied because not all ranges of time are available for inclusion in the calculation. The values of t at which K(t) is calculated are relatively small, and hence the weighting factor should have little effect. To substantiate this it was observed (8) that the average change in K-values at t equal to 100 seconds, due to the weighting factor, was less than 5%. A more detailed explanation of W_{ij} for time distributions and time sequences has been provided (8).

In the observation of behavior, acts do not occur in isolation, but instead are performed in a structured order. These acts may be related to each other. This relationship may be partly random, or it may be partly deterministic, in that the occurrence of a particular act depends upon the occurrence of a preceding act. To assess sequences of acts and their multivariate relationships, the K-function was introduced (8) for the joint acts α and β defined as:

$$K_{\alpha\beta}(t) = (N_\alpha N_\beta)^{-1}\tau_{\alpha\beta}\left\{\sum_{i=1}^{N_\alpha}\sum_{j=1}^{N_\beta} W_{ij}^{-1} I_t(U_{ij}^{\alpha\beta})\right\} \quad (3)$$

Each term has a meaning similar to that discussed for Eq. (1). In this use $\tau_{\alpha\beta}$ is corrected for the extension of each of the two different acts for the sequence analysis and becomes:

$$\tau_{\alpha\beta} = (T - t_\alpha - t_\beta) + N_\alpha + N_\beta \quad (4)$$

In Eq. (4) the meaning of each term is the same as in Eq. (2).

In Eq. (3) the $U_{ij}^{\alpha\beta}$ is the separation between the i-th event of act α and the j-th event of act β. The $I_t(U_{ij}^{\alpha\beta})$ term is changed to fit the behavioral sequence situation. In order to retain information on possible causal relationships among the acts the formulation is intentionally and specifically asymmetric in the time relationship. The term $I_t(U_{ij}^{\alpha\beta})$ equals 1 if event j of act β occurs within a time interval t later in time than event i of act α, and $I_t(U_{ij}^{\alpha\beta})$ equals 0 if event j occurs earlier than event i or if the time separation exceeded t. That is, the sum over j is only for events of act β later than event i of act α.

Whenever any time distribution or sequence involved a behavioral act that had an average number of initiations (per animal) less than ten in either the control or exposed group, they were excluded from the analysis.

Estimates of the uncertainty in K(t). The function K(t) is computed, for any data set, from the observation of p pairs of animals. Each animal is half of a pair composed of one control and one exposed animal. The set of data from p control and p exposed animals is used to calculate a ΔK(t) [the difference between K(t) for the control and the exposed groups] for a given time value t. The replication involving p such pairs allows the use of the bootstrap technique to estimate the standard deviation in a measure of interest. This technique (1, 3–6) uses Monte Carlo methods to generate an estimate of the variance of a statistic based only on the data. A random number generator is used to construct one thousand simulations of this calculation. In each instance a list of p pairs, randomly selected from the original set of animal pairs, is generated. Obviously one or more pairs may be dropped in any one of these simulations while others are included more than once. Standard statistical formulae can then be used on all of the simulations to obtain an estimate of the standard deviations of K(t) for the control and exposed groups separately or of ΔK(t).

Criteria for the significance of observed change. The calculation of K(t) involves all pairs of an act separated by a time less than or equal to t. Certain discrete values of t, at which the K-function is calculated, are selected (t = 2, 5, 10, 20, 30, 45, 100, and 200 seconds). Each time distribution [Eq. (1)] or time sequence [Eq. (3)] is quantified by the appropriate K-function calculated at these eight time points. Although it would be straight forward to appropriately define a condition for stating that the value of K(t) is significantly changed, between the control and exposed groups, at any particular time point, this would not necessarily correspond to a change in the K-function for these groups. Any criteria used to label a change in the K-function as "real" will, of necessity, be of an ad hoc nature [for further discussion on this matter see (8)]. In determining that a time distribution or time sequence, by which we mean the K-function evaluated at each of the eight time points for each treatment group, should be flagged as corresponding to a "real" change between control and exposed groups, multiple tests must be simultaneously satisfied. First, the following quantity is evaluated for each point:

$$\frac{|K_{exp}(t) - K_{con}(t)|}{St.dev\,[K_{exp}(t) - K_{con}(t)]} = \frac{|\Delta K(t)|}{St.dev\,[\Delta K(t)]} \quad (5)$$

In Eq. (5) K(t) has the meaning defined in Eq. (1) or Eq. (3). The subscripts "exp" and "con" refer to the exposed and control groups. Here ΔK(t) represents the difference between exposed and control groups, and St. dev[ΔK(t)] represents the estimated standard deviation in this measure derived from the bootstrap calculation. Second, the given time distribution or sequence is not flagged as corresponding to a "real" change unless the value

calculated in Eq. (5) is greater than or equal to 2.0 for three adjacent time points. Third, these three time points must have the same sign for $\Delta K(t)$.

RESULTS

Analysis of Group Acts

Control experiment. Twenty-five time distributions or sequences fulfilled the conditions for analysis. Of these 25, two satisfied the conditions to be flagged as "real" changes. This corresponds to a false-positive rate of 8%. However, this rate should be treated as somewhat uncertain since the estimate depends upon the data from a single experiment.

An additional point relative to the uncertainty in the false-positive rate merits discussion. The methods used for these calculations result in the possibility of sampling fluctuations in the estimate of the standard deviation provided by the bootstrap calculation. Such sampling fluctuations could be reduced by using more animal pairs or by increasing the 1000 iterations of the bootstrap by a large factor. Both methods are expensive. Both the size and the effects of such sampling fluctuations can be empirically examined by reanalyzing the data using a different set of 1000 listings of the animal pairs. This can be done by using a different initialization value for the random number generator. Changes which appear or disappear with different initialization values in such repeated examinations are very marginal. With experience in interpreting these results it is possible to quickly identify such marginal signals even without repeating the entire analysis. The data from the control experiment were reanalyzed five times, sometimes yielding one "real" change sometimes two. One such change (the time sequence calculations for "groom/explore" with "explore") was consistently present and occasionally one of two others was flagged as a "real" change. By presenting a different analysis, the false-positive rate could have been quoted as one out of 25, or 4%. We have chosen to present the more conservative 8% value. This discussion shows the uncertainty in this estimate. More details for identifying marginal signals and for more stringently defining a "real" change will be discussed later.

Amphetamine experiment. Sixteen time distributions or sequences fulfilled all of the conditions for analysis. The average initiations per animal of the act "groom/explore" was approximately 7 for the exposed group; therefore, the time distribution for this act and the 8 time sequences which involved this act were dropped from the analysis. Of these 16 K-calculations, 8 were flagged as "real" changes in the amphetamine-treated animals. If we assume: 1) that all 16 distributions or sequences are independent, 2) an 8% false-positive rate, 3) a null result is used for test purposes, and 4) an approximate binomial distribution for the number of "real" changes, then the summed binomial distribution function can be used to calculate the probability that these results are in agreement with the null hypothesis. The p-value which results from this calculation is 0.000012, a clear rejection of the null hypothesis.

To demonstrate the observed changes, the value of $\Delta K(t)$ for the first six time points is shown in Fig. 1 plotted against time for the time sequence of the group acts "attention" and "explore." These calculations result from the use of Eq. (3).

Additional aspects of "real" changes. Examination of the results presented here and in the two earlier reports (8,10) revealed other systematic differences between many of the changes involved in the false-positive signals and those observed when behavioral changes are expected. These differences could be used to tighten the criteria for a "real" change and thus reduce the reported false-positive rates. This discussion demonstrates that this analysis technique and the criteria used are still being developed and the criteria may be refined or changed in the future.

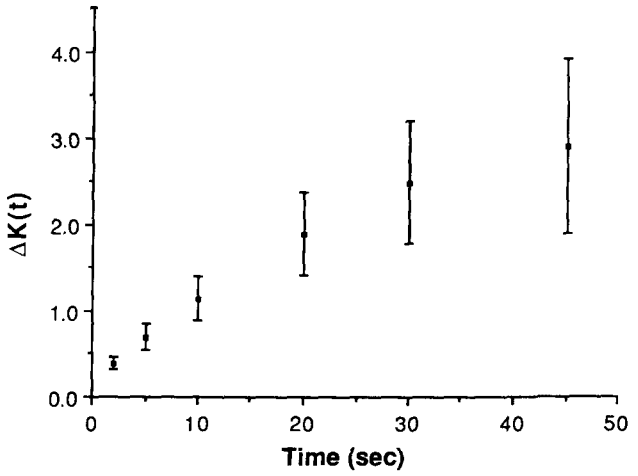

FIG. 1. $\Delta K(t)$ for the time sequence of the group acts "Attention/Explore" ($\pm$ SD) at the first six time points at which this is evaluated. The results shown are for the data in the 2.0 mg/kg amphetamine study.

First, we will consider the effect of sampling fluctuations in the estimate of the standard deviation of $\Delta K(t)$. For a value of Eq. (5) near 2.0, the typical sampling fluctuation found with repeated calculations is approximately ± 0.1. Cases where this variation has exceeded ± 0.2 have not been observed. Therefore, if on the first such calculation, three adjacent time points exceed 2.2 for the value of Eq. (5), it is extremely unlikely that this change will not satisfy the conditions for a "real" change on any calculation with a different seed number. Alternatively, any act which on the first calculation had three adjacent time points where the value from Eq. (5) exceeds 1.9, is an act which on subsequent calculations might be flagged as a "real" change.

Second, consider the effect of which time points satisfy the condition that the value for Eq. (5) exceeds 2.0. The great majority of "real" changes found in the positive experiments [the amphetamine experiment reported in this paper and the nitrous oxide and phenytoin experiments analyzed in previous studies (8,10)] satisfy this condition in the first three discrete time points. Most of the reported false-positive signals do not satisfy this condition until the time equals or exceeds 20 seconds. This is illustrated in Fig. 2 where the values of $\Delta K(t)$ for the group act "attention" are plotted versus time for all eight time points. This group act is one of two flagged as a "real" change, where that flagging is not consistent upon repeated calculations, that is, it is a marginal signal affected by sampling fluctuations. To emphasize the difference, seven of the eight "real" changes reported in the amphetamine experiment satisfy the condition that the value calculated for Eq. (5) exceed 2.0 for the first time point.

Analysis of the Full Taxonomy

Control experiment. Fifty-two time distributions or sequences fulfilled the conditions for analysis. Of these, 5 met the criteria for "real" changes. Based upon this information alone, the false-positive rate would be estimated at approximately 10%. In view of the previous discussion, the time of onset of these five signals was noted. One began at each of the following time points: 2, 10, 20, 30 and 45 sec. Three of the 5 signals have a time of onset greater

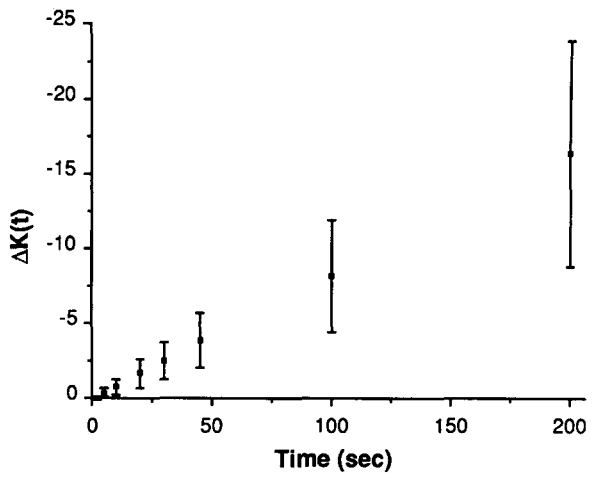

FIG. 2. ΔK(t) for the group act "Attention" (±SD) at the eight time points. The results shown are from the control experiment.

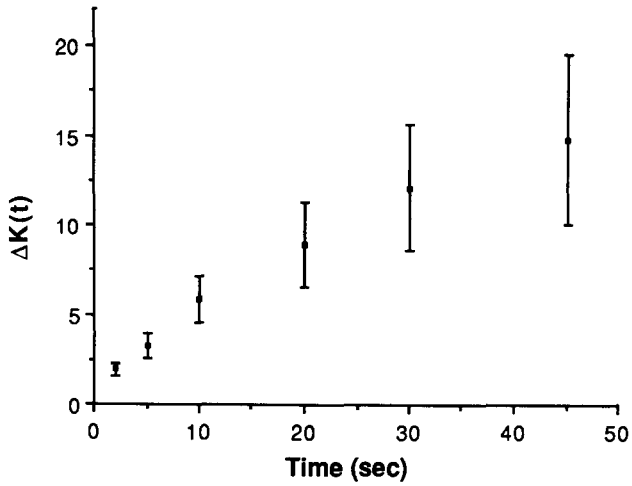

FIG. 3. ΔK(t) for the time sequence of the major body positions "Rear/Walk" (±SD) at the first six time points at which this is evaluated. The results shown are for the data in the 2.0 mg/kg amphetamine study.

than or equal to 20 seconds, suggesting that such signals beginning late in time may preferentially be "noise" or false-positive signals.

Amphetamine experiment. Forty-one time distributions or sequences fulfilled all of the conditions for analysis. Of these 41 K-calculations, 22 were flagged as "real" changes in the amphetamine-treated animals.

A comparison of the time of onset of these 22 "real" changes and the 5 "real" changes observed in the same analysis for the control experiment is presented in Table 2. These data clearly show a difference in the distribution of the time of onset of false-positive signals and those signals associated with amphetamine exposure.

To illustrate the observed changes, the value of ΔK(t) for the first 6 time points is shown in Fig. 3 plotted against time for the time sequence of the acts "rear" and "walk." Shown in Fig. 4 are the values of ΔK(t) plotted against time for the same 6 time points for the time sequence of the modifier acts "look" and "turn." Comparison of Figs. 1, 3, and 4 reveals a striking similarity in the form of the amphetamine disruption in these various sequence calculations.

The summed binomial distribution function can be used to calculate the probability that these results are in agreement with the null hypothesis. The necessary assumptions are: 1) that the null hypothesis is used for test purposes; 2) the distribution for the number of "real" changes is approximately binomial; 3) that all 41 distributions or sequences studied can be treated as independent; and 4) the estimate for the false-positive rate is 10%. The p-value calculated is less than 0.0001, a clear rejection of the null hypothesis.

TABLE 2

Full List of Acts

	Time Point	1	2	3	4	5	6	Total
	Time Value (Sec)	2	5	10	20	30	45	all
Experiment	Number of time distributions or sequences studied							
Amphetamine	41	20	1	0	0	0	1	22
Control	52	1	0	1	1	1	1	5
Estimated false positive rate (percent)		2	2	4	6	8	10	10

Group Acts

	Time Point	1	2	3	4	5	6	Total
	Time Value (Sec)	2	5	10	20	30	45	all
Experiment	Number of time distributions or sequences studied							
Amphetamine	16	7	0	0	1	0	0	8
Control	25	0	1	0	0	0	1	2
Estimated false positive rate (percent)		0	4	4	4	4	8	8

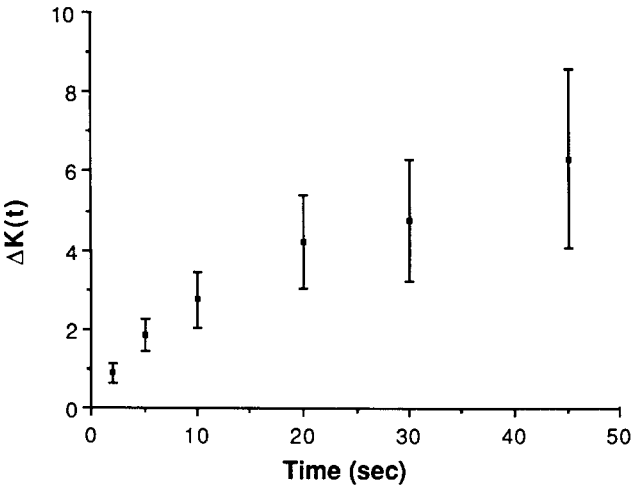

FIG. 4. ΔK(t) for the time sequence of the modifiers "Look/Turn" (± SD) at the first six time points at which this is evaluated. The results shown are for the data in the 2.0 mg/kg amphetamine study.

A decrease in the value of K(t) corresponds to the act becoming more dispersed in time, while an increase in K(t) corresponds to the act becoming more clustered in time. A natural question that emerges is how the 22 "real" changes reported for the amphetamine exposure distribute between these two possibilities. Of the 22 "real" changes, 19 correspond to a decreased value of K(t) in exposed animals when compared with control animals, and only 3 correspond to the reversed situation.

DISCUSSION

This study has taken data collected and classified with the RAPID system and applied the technique of the K-functions to study the time structure of behavioral acts. The control experiment was specifically designed to produce estimates of the false-positive rates for data obtained with the RAPID system. In the analysis of the "group" acts, the estimate of the false-positive rate was 8%. It was also pointed out that various systematic differences between the false-positive signals and those observed in the amphetamine experiment could be used to reduce the false-positive rate. One such additional discriminant was the time of onset of the signal. The analysis of the full taxonomy for Experiment 1 showed that the estimated false-positive rate was 10%, but again the estimate of this rate could decrease depending upon the use of time of onset of the signal.

When the "group" acts were studied with the K-functions for the amphetamine experiment, 8 of the 16 (50 percent) time distributions or sequences met the criteria for "real" changes. This result clearly rejects the null hypothesis. When the full taxonomy of acts was analyzed with the K-functions, 22 of the 41 time distributions or sequences studied met the criteria for "real" changes. Again, the null hypothesis was clearly rejected even without an effort to further reduce the estimate of the false-positive rate.

In Figs. 1, 3 and 4 it was shown that many of the disruptions of time structure due to amphetamine were strikingly similar in shape as a function of time. For the full taxonomy it was shown that 19 of the 22 "real" changes corresponded to increased dispersion of the act in time, and for the group acts a similar increase in dispersion was observed in 7 of 8 "real" changes.

The independence of the results of the time distribution of an act and the time sequences which involve that act, be it the initiator or the second act, has been considered (10). The majority of the evidence regarding this point is taken from the analysis of the full taxonomy. The time distribution of the body position sit is flagged as a "real" change; those for stand, rear and walk are not. In fact, none of these latter 3 acts are close to the criteria for a "real" change. Only 2 of the 24 time points have a value for Eq. (5) greater than 2.0, and although both are in the distribution for rear, they are widely separated (being the first and seventh time points). Of the 12 time sequences studied involving body positions, 2 of the 6 involving sit are flagged as having "real" changes. Five of the other 6 time sequences for body positions are flagged as changed, but none of the acts involved in these sequences had altered time distributions. The time distribution for the body position rear is not flagged as a "real" change, but all 6 time sequences involving rear are flagged as having "real" changes. When the time distributions of the modifiers were examined, 4 of the 5 distributions were flagged as "real" changes. Of the 20 time sequences studied for the modifiers, all involve at least one act from the 4 which were changed, but only 10 of the sequences were flagged as corresponding to "real" changes. Clearly, the results of a particular time sequence calculation cannot be completely predicted based upon knowledge of the time distributions of the two acts involved in the sequence. The sequence calculation is at least partially independent of the distribution calculations.

When additional data from the RAPID system becomes available, a more comprehensive effort to establish the false-positive rates will be undertaken. In the interim, the results presented here establish estimates that are acceptable and, as shown by the amphetamine data, the system can readily detect changes associated with exposure of the animals to agents which cause behavioral disruption. RAPID is different from other behavioral tests. It is a fully automated system with a built in degree of behavioral classification and data analysis yet to be achieved with any other activity device.

REFERENCES

1. Diaconis, P.; Efron, B. Computer intensive methods in statistics. Sci. Am. 248:116–130; 1983.
2. Diggle, P. J. Statistical analysis of spatial point patterns. New York: Academic Press; 1983.
3. Efron, B. Bootstrap methods: Another look at the jackknife. Ann. Stat. 7:1–26; 1979.
4. Efron, B. Computers and the theory of statistics: Thinking the unthinkable. Soc. Indust. Appl. Math. Rev. 21:460–480; 1979.
5. Efron, B. The jackknife, the bootstrap and other resampling plans. Philadelphia: Society for Industrial and Applied Mathematics, Monograph #38; 1982.
6. Freedman, D. A.; Peters, S. C. Bootstrapping a regression equation: Some empirical results. J. Am. Stat. Assoc. 79:97–106; 1984.
7. Kernan, W. J.; Mullenix, P. J.; Hopper, D. L. Pattern recognition of rat behavior. Pharmacol. Biochem. Behav. 27:557–564; 1987.
8. Kernan, W. J.; Mullenix, P. J.; Kent, R.; Hopper, D. L.; Cressie, N. A. C. Analysis of the time distribution and time sequence of behavioral acts. Int. J. Neurosci. 43:35–51; 1988.
9. Mullenix, P. Effect of lead on spontanious behavior. In: Needleman, H. L., ed. Low level lead exposure: The clinical implications of current research. New York: Raven Press; 1980:211–220.
10. Mullenix, P. J.; Kernan, W. J. Extension of the analysis of the time structure of behavioral acts. Int. J. Neurosci. 44:251–262; 1989.
11. Mullenix, P. J.; Moore, P. A.; Tassinari, M. S. Behavioral toxicity of nitrous oxide in rats following prenatal exposure. Toxicol. Indust. Health 2:273–287; 1986.
12. Mullenix, P.; Tassinari, M. S.; Keith, D. Behavioral outcome after prenatal exposure to phenytoin in rats. Teratology 27:149–158; 1983.

13. Norton, S. Amphetamine as a model for hyperactivity in the rat. Physiol. Behav. 11:181–186; 1973.
14. Norton, S.; Mullenix, P.; Culver, B. Comparison of the structure of hyperactive behavior in rats after brain damage from x-irradiation, carbon monoxide and pallidal lesions. Brain Res. 116:49–67; 1976.
15. Ripley, B. D. The second-order analysis of stationary point processes. J. Appl. Probabil. 13:255–266; 1976.
16. Ripley, B. D. Spatial statistics. New York: John Wiley and Sons; 1981.