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Age Differences in Locomotor Behavior of C57BL/6NNia Mice: A Data Management Approach

MICHAEL J FORSTER

Department of Pharmacology, Texas College of Osteopathic Medicine
Camp Bowie at Montgomery, Fort Worth, TX 76107-2690

FORSTER, M J *Age differences in locomotor behavior of C57BL/6NNia mice A data management approach* PHARMACOL BIOCHEM BEHAV 27(3)545–551, 1987 —Separate age groups of C57BL/6NNia mice were tested for within- and between-session habituation of locomotor behavior using a Digiscan System for simultaneous automated gathering of 23 locomotor variables A computer program, *R*aw *D*ata *I*nput *P*rogram (RDIP) was developed for the reformatting and transfer of raw data samples to a spreadsheet/database management system, and a method for summarization, analysis and presentation of the multivariate data is described It is concluded that large samples of multivariate locomotor activity data can be effectively managed using a single microcomputer and commercially available software packages

Locomotor activity Automation Habituation Data management Statistical analysis C57BL/NNia mice Digiscan

MEASUREMENT of locomotor behavior has long been recognized as an important tool in animal behavior research and has many applications to the study of senescence in animals Measurement of locomotor activity in various contexts has been employed to test hypotheses about age differences in arousal [7], exploration [4] and simple nonassociative learning and memory processes [2, 3, 5, 6] Moreover, the effects of pharmacologic agents upon locomotor activity have been employed as probes for identification of neurological changes in aging [8, 9, 13] Unfortunately, interpretation of age-related locomotor activity changes in terms of neurological mechanisms or constructs such as exploration, arousal, and memory is almost never straightforward, because of the large number of factors influencing spontaneous activity which also interact with aging Rigorous parametric and descriptive analyses of the phenomena under investigation can often facilitate interpretation, but such analyses require an experimental effort which grows exponentially with the number of age groups and variables which must be introduced

Apparatus designed for description and simultaneous automated measurement of many components of locomotor behavior [1,10] have the potential to greatly reduce the experimental effort involved in such studies, and will no doubt afford greater insight into those elements of behavior which are affected in aging Unfortunately, in many descriptive/parametric applications, the unwieldy size of the data sample engendered by the use of these apparatus can severely impede the process of inspection and analysis of data Depending upon the human and material resources at the experimenter's disposal, he/she may be tempted not to exploit the full power of multivariate analysis in the interest of expediency However, many apparatus generating multiple activity dependent measures operate using a microcomputer, and with the availability of sophisticated database management and statistical packages for these computers, the collection, inspection, analysis and graphic presentation of multivariate data can be done using the same computer This paper outlines such a method as it was applied to multivariate locomotor activity data generated by a Digiscan Animal Activity Monitoring System A simple descriptive analysis of age-dependent changes in between-session habituation is used to illustrate the processes of data handling

THE EXPERIMENTAL PROBLEM

Numerous investigations of locomotor behavior in aged rodents have suggested impairments of habituation and deficits in the retention of habituation with increasing age [2, 3, 5, 6] These studies have examined habituation by different methods, each involving univariate measures of spontaneous activity or exploration In order to provide a complete descriptive analysis of life-span changes in habituation of locomotor behavior, mice of various ages were compared for between- and within-session habituation using apparatus for multivariate activity measurement The immediate goals were to determine if habituation impairments could be detected using such an apparatus and to identify the specific behavioral components involved However, the experimenter envisioned a continuing program of study in which several mouse strains would be compared for age differences across multivariate measures Such a research program would generate a large body of data to be collected under

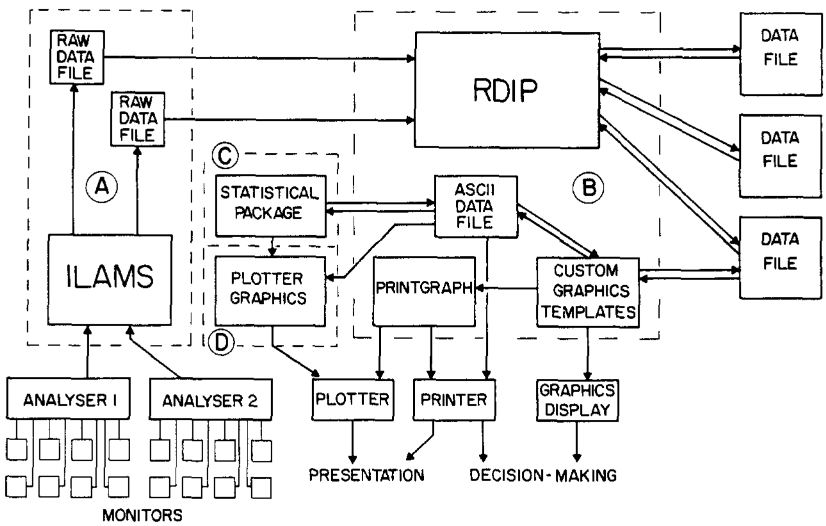

FIG 1 Organization of software and hardware for management of locomotor activity data In (A), the output of the Digiscan analysers is written to disk using Integrated Laboratory Animal Monitoring System (ILAMS) software In (B), the raw data files written by ILAMS are imported into the Lotus system, reformatted, and stored using Raw Data Input Program (RDIP), a Lotus 1-2-3 dependent program Analysis and presentation is done within the Lotus-1-2-3 environment (B) or by creating ASCII files within Lotus to be used by other software (C), (D)

many parameters, and it was therefore necessary to organize a system for data management which could be used routinely in subsequent investigations Data collection, storage, analysis, and presentation will be described below as it applied to 5 separate age groups of C57BL/6NNia mice (1–2, 2–4, 5–7, 11–13, or 24–28 months) Each group of mice was tested for between-session habituation by administering 20-minute locomotor activity tests on each of 6 successive days Within-session habituation was assessed by sampling activity within each of four 5-min periods

EQUIPMENT

Hardware

Locomotor activity was monitored using a Digiscan Animal Activity Monitoring System (Omnitech Electronics, Inc , Columbus, OH) which consisted of individual acrylic activity cages (40×40×30 5 cm) surrounded by red-filtered horizontal and vertical activity sensors [Model RXYZCM(8)], and a Digiscan Analyser (Model ACM) for collection and initial sorting of locomotor variables This apparatus utilizes 24 infrared photocell beams to generate 7 measures related to ambulation [10], 3 related to rearing [12], 2 measures of stereotypy [11], and 2 measures of rotational behavior In addition, the apparatus allows quantification of the amount of time spent in any of 9 equal floor zones for a total of 23 dependent measures The operation, utility, and reliability of the Digiscan system has been discussed previously [10]

All hardware and software operations were done using an IBM Personal Computer (PC) XT model 5160 (International Business Machines, Armonk, NY) running IBM PC DOS version 3 1 or 2 0 The IBM PC had one 10 M-byte fixed disk drive, one dual-sided diskette drive, 256Kb of motherboard random access memory (RAM), and an Intel Corp (Hillsboro, OR) 8087 numeric data processor The microcomputer was also equipped with an Amdek Corp (Elk Grove Village, IL) video monitor (Model 310A) and several add-on cards Data were passed from the Digiscan Analyser to the IBM PC using an Omnitech, Inc Dual Interface Card located in expansion slot 1 Software graphics applications were accomplished with the aid of Hercules Computer Technology (Berkeley, CA) monochrome (model GB101) and color (model GB200) graphics cards located in slots 2 and 3 of the PC A JRAM-3 (model B1150, Tall Tree Systems, Palo Alto, CA) memory expansion board in slot 3 provided an additional 384Kb of system RAM and approximately 1 7 Mb of expanded memory specification (EMS) accessible RAM for use by the data management software Graphics were printed using an Epson Corp (Nagano, Japan) model FX-80 printer and/or a Hewlett-Packard (Palo Alto, CA) model 7475A plotter

Software

The software and their functional interactions are depicted in Fig 1 Transfer of Digiscan activity measures to the fixed disk of the IBM PC was accomplished using Integrated Lab Animal Monitoring System (ILAMS) (Fig 1A) software version 2 0 (Omnitech Electronics, Columbus, OH) *R*aw *D*ata *I*nput *P*rogram (RDIP) (M Forster), a Lotus-dependent program, was used to transfer and reformat raw data files for their subsequent manipulation within Lotus 1-2-3 version 2 01 (Lotus Development Corp , Cambridge, MA) (Fig 1B) Sigma-Plot (Jandel Scientific, Sausalito, CA) was used for generation of quality graphs (Fig 1D) and Ganova (M Brecht and J A Woodward, Venice, CA) was used to perform Analyses of Variance (Fig 1C)

DATA COLLECTION

Collection of locomotor activity data was initiated through ILAMS, a BASIC program which writes a file in

```
[Input]  Retrieve  Enter  Save  Load  Hold  Format  Quit
Import, Keyboard, Page, Clear, Delete, Sort, Reset
      BY   BZ   CA   CB   CC   CD   CE   CF   CG   CH   CI   CJ   CK   CL
1   @@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@
2   @@@@@ DATA ENTRY AND IMPORT UTILITY:    8- or 16-beam Digiscan    @@@@@
3   @@@@@                                   System                    @@@@@
124 @@@@@          Michael J. Forster                 10-1-86         @@@@@
125 @@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@@
126
127
128
129      ENTER CHOICES BY ARROW KEY HIGHLIGHTING/RETURN
130      OR BY TYPING FIRST LETTER OF CHOICE
131
132
133
134               QUEUED RECORDS=   0
135               RESIDENT FILE: NONE
136               IMPORT FILE # =NONE
137               DATA FORMAT =  8-BEAM
138
139
140
27-Oct-86  12:24 PM                          [CMD]
```

FIG 2 Opening menu of RDIP Raw data files are imported, reformatted, sorted, and directed to different storage files by highlighting pre-programmed menu options (see text)

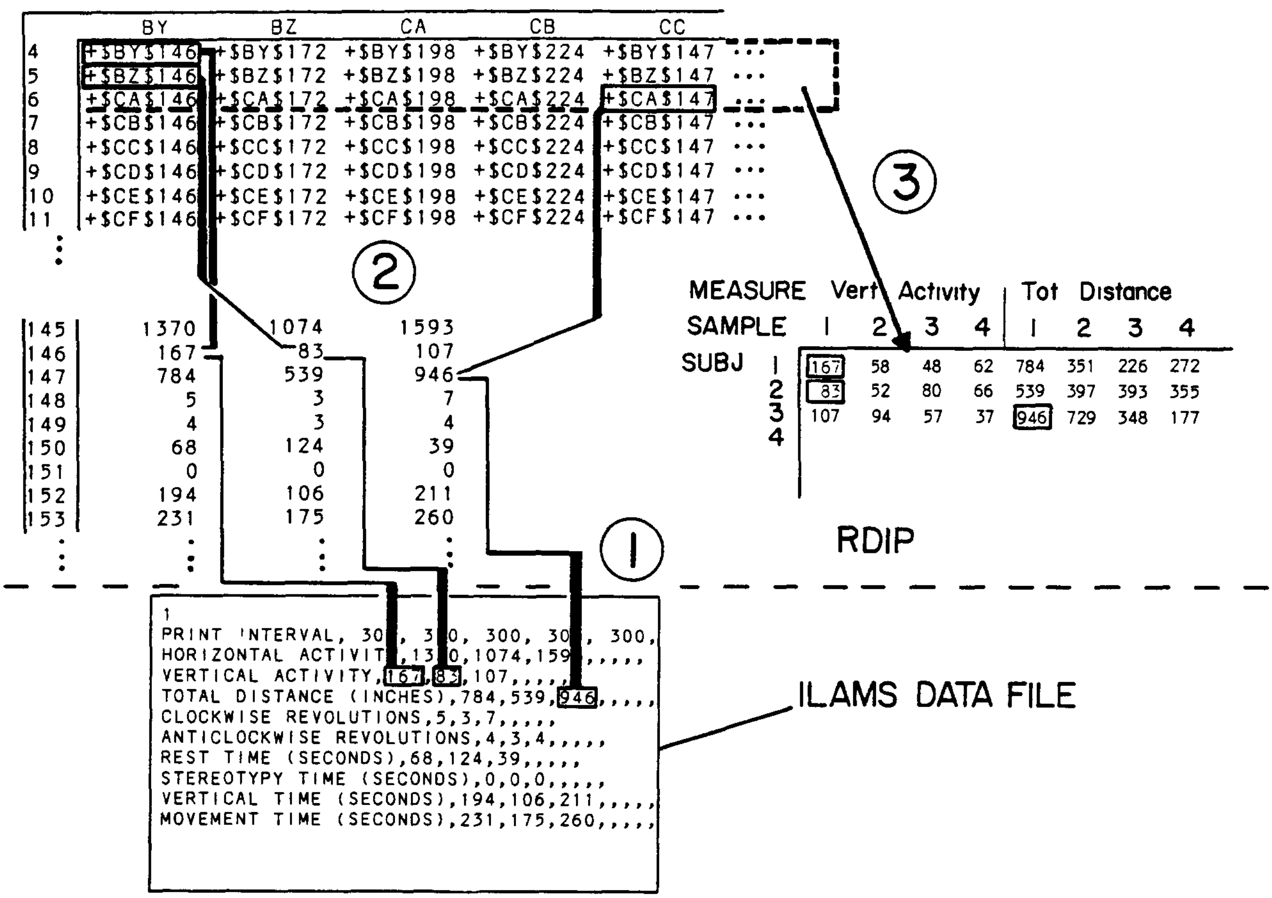

FIG 3 Method for reformatting raw data files (1) Lotus commands / *F*ile *I*mport *N*umbers cause labels to be dropped and the raw data appear in separate columns within RDIP (2) Specially juxtaposed formulas address and display the incoming data in the desired format (3) Values displayed by the formulas are copied to a temporary storage area by the Lotus commands / *R*ange *V*alue

A157: 69 READY

	A	B	C	D	E	F	G	H
1	Vert. act.				Tot. dist.			
2	1	2	3	4	1	2	3	4
3	=====	=====	=====	=====	=====	=====	=====	=====
157	69	62	69	67	323	262	172	197
158	58	50	43	50	280	237	220	141
159	53	32	55	54	408	212	166	221
160	59	65	66	72	455	220	178	127
161	34	29	16	5	251	154	99	29
162	59	44	27	45	453	197	116	155
163	39	71	49	69	346	260	126	156
164	15	15	0	0	137	74	0	29
165	21	36	37	29	208	172	206	126
166	31	32	28	46	326	216	249	137
167	17	27	24	20	347	196	254	133
168	12	27	10	9	185	158	63	127
169								
170								
171								
172								
173	=====	=====	=====	=====	=====	=====	=====	=====

	BH	BI	BJ	BK	BL	BM BN
1	SUBJECT INFORMATION					
2	#	Code				Cell
3	=====	M	A	T	-S	=====
157	B09	1	2	2	1	
158	B10	1	2	2	2	
159	B05	1	2	2	3	MAIN
160	B06	1	2	2	4	CELL:
161	A09	1	2	2	5	
162	A10	1	2	2	6	C57BL/6Nnla
163	A06	1	2	2	7	2-4 mo
164	A08	1	2	2	8	
165	A03	1	2	2	9	Test 2
166	A05	1	2	2	10	
167	B07	1	2	2	11	
168	B08	1	2	2	12	
169						
170						BUFFER
171						CELL
172						
173	=====	=====	=====	=====	=====	=====

27-Oct-86 12:38 PM

FIG 4 Data storage file The left and right extremes of the Lotus worksheet are shown in separate windows The right window always displayed subject identification as the user scrolled up-down or right-left to view any "cell" of the experimental design

standard ASCII format to any disk of the microcomputer Using ILAMS it is possible to receive data from 2 Digiscan analysers running simultaneously, each connected to up to 8 monitors (see Fig 1A) The number of samples to be gathered and the drive, path and filename where the data were to be stored were entered following simple prompts to the experimenter During testing, the status of data collection for each analyser was monitored on a real-time display, and data files could be viewed on screen as they were output from the analyser Before starting a session, the experimenter used a routine of recording the animal identification specifics and the experimental conditions represented by a "run," together with the name of the file to be generated All data files were designated with the file extension "prn" (i e , DT1 prn, DT2 prn) and stored in a subdirectory "\ILAMS" on the fixed disk of the IBM PC, which also contained the ILAMS program

DATA STORAGE

Requirements

It was desirable to have data stored in an analysis of variance table format so that minimal re-organization of data would be required prior to analysis using statistical packages, and so that the experimenter could view data in a familiar format Another requirement was that the experimenter be able to report and discuss the results of experiments on a variety of measures on a day-to-day basis, as data were being collected These goals were accomplished using Lotus 1-2-3 (Fig 1B), a commercially available database management/graphics program which allows storage and manipulation of data in specially formatted files or "worksheets " Each worksheet had a labeled 256 column × 8192 row working area in which each cell was individually addressable Lotus 1-2-3 has the capability of reading external ASCII files, reformatting their contents using a variety of commands, and writing new files in ASCII format compatible with statistical and graphics packages Lotus 1-2-3 commands were initiated by "/" keystroke, after which the user could make selections from hierarchically organized menu alternatives for editing and manipulation of data Long sequences of Lotus commands could be programmed to initiate automatically after special keystrokes or following their selection from menus of the user's own design These customized worksheets could be stored and re-used as functional, Lotus-dependent programs The Lotus system permitted error-trapping, disk operations, and opening of other Lotus files within these programs

Importation of ILAMS Data Files to Lotus 1-2-3

In order to permit routine transfer and reformatting of data for use by Lotus 1-2-3, it was necessary for the experimenter to design RDIP (shown in Fig 1B), a Lotus-dependent program which was permanently stored on the fixed disk of the IBM-PC RDIP performed three major functions First, ILAMS data files were imported to the Lotus system and converted to analysis of variance format (data could also be entered efficiently from the keyboard if necessary) Individual records (all samples and dependent measures from one subject) were then tagged with proper identification and held in temporary storage such that the user could access individual records, and sort the records according to their eventual destinations Third, each record in temporary storage was entered as a unit to the appropriate location in any one of several destination files (for permanent storage), which could be loaded from and saved to floppy disks In order to use RDIP, the experimenter had to load the Lotus system and retrieve the RDIP program file using Lotus commands Upon retrieval, a series of experimenter-defined menu choices were displayed (see Fig 2) Menu choices were made by highlighting the appropriate option and de-

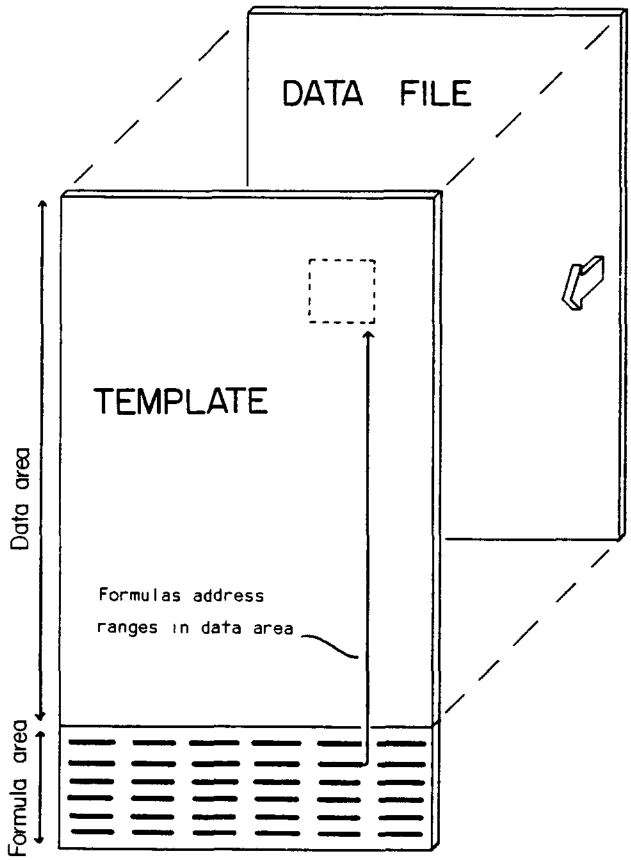

FIG 5 Summarizing data from storage files Templates compatible with any storage file contained Lotus formulas, pre-formatted graphs (lower portion of template), and a blank data area (upper portion of template) The Lotus commands / *F*ile *C*ombine *C*opy *E*ntire file, allowed a file containing data to overlay the template data area, permitting the display of updated tables and graphs

pressing the return key, or by typing the first letter of the menu choice Selection of a menu option activated the long series of Lotus commands used by RDIP to reformat and transfer the ILAMS files to the Lotus system As shown in Fig 2, the display informed the experimenter as to how many data records had been reformatted and put into temporary storage (queued records), the name of the destination file which was currently in memory (resident file) and the name of the ILAMS data file which had most recently been imported (import file) The data format display (Fig 2) showed which type of data file RDIP could currently reformat This was included because two types of Digiscan apparatus are in use in this laboratory which produce data files of different formats A menu option allowed the user to toggle between the different data formats

Reformatting Raw Data Files

The method used by RDIP for importing and reformatting the ILAMS raw data files is shown in Fig 3 Each raw data file reflected the ordering of data as it was passed from the Digiscan analyser, with time-sampling periods appearing in sequence from top to bottom Each time-sample grouping contained alphabetical labels for each dependent measure and the corresponding numeric data for monitors 1–8 (delimited by commas) on a separate line In (1), the Lotus commands / *F*ile *I*mport *N*umbers, allowed the user to first choose and then import data files from a menu of files contained in the "\ILAMS" directory of the fixed disk The alphabetical labels were dropped during this process and the numbers for each monitor appeared in separate columns of a designated free area of the worksheet

Reformatting the data, once imported, involved changing the columns into rows and then re-structuring those rows such that the 4 samples of a given dependent measure appeared in sequence from left to right in one area of the record This was accomplished [in (2)] by rows of Lotus formulas which addressed and displayed the current values of cells in the area of the worksheet where the ILAMS file had been imported The text of these formulas is shown at the top of Fig 3 Each formula consisted of a cell address, for example, the formula at the extreme upper left addressed and displayed the contents of a cell at the intersection of column BY and row 146 By virtue of the positions of the formulas in the rows, a new ordering of the data in the imported file was created and displayed in the formulas area In (3), the reformatted data displayed in the formulas area (but not the formulas) were copied to the temporary storage area using the Lotus menu commands / *R*ange *V*alue The whole process was repeated each time a new raw data file was imported A library of differently ordered cell address formulas for different formatting applications was stored on the fixed disk of the IBM-PC, and could be installed in RDIP to create different orderings of the data records, skip some Digiscan variables, transform selected measures, or create new measures derived from the incoming variables as they were imported In the present investigation, 13 variables were transferred by RDIP Total distance, vertical activity, total revolutions, stereotypy time, vertical time, movement time, number of stereotypy, number of vertical movements, number of movements, center time, average speed of movement, and average distance per movement (for discussion of these measures see [11]) One measure, "non-corner time," was derived from the individual zone times as the ILAMS file was imported This measure reflected the total time spent in all but the corner zones and was calculated as follows

Non-corner time = left-center time + right-center time + center-front time + center-rear time + center time

Transfer to Storage Files

Menu options in RDIP allowed the experimenter to select large storage files from floppy disks as destinations for the data records in temporary storage The program used the Lotus commands / *F*ile *C*ombine *C*opy *E*ntire file, to "load" a destination storage file from one disk Additional menu choices then allowed the user to view the destination file and the new data records simultaneously in 2 windows, and transfer each record as a unit from temporary storage to the appropriate cells of the storage file When this process was complete, a menu option allowed the updated version of the storage file to be saved to the floppy disk To accomplish this, RDIP used the Lotus commands / *F*ile *X*tract *F*ormulas If several experiments were being conducted simultaneously, the data records which were intermixed in temporary storage could be sorted, or individually directed to appropriate storage locations by consecutively loading, updating, and saving the appropriate storage files

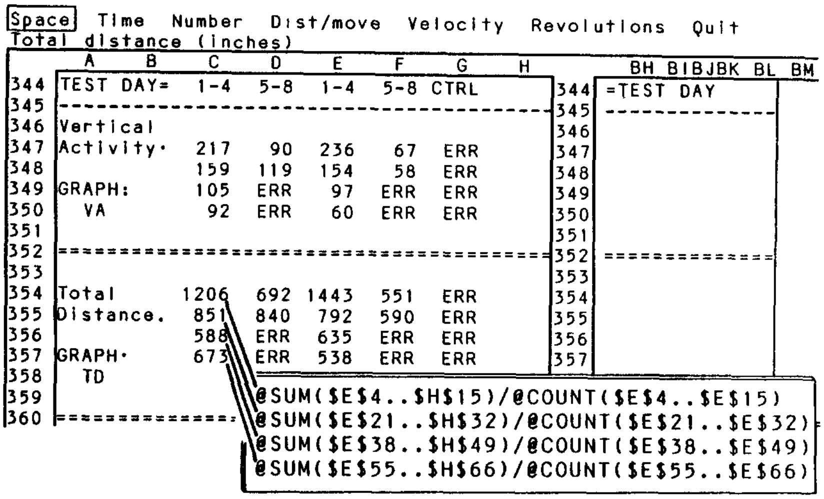

FIG 6 Data summary table and graphs menu Summary tables consisted of Lotus formulas addressing appropriate cells in other areas of the worksheet (see text) Menu options permitted displaying of graphs and their corresponding tables

DECISION-MAKING AND COMMUNICATION

Once the data had been stored in proper format, Lotus 1-2-3 commands were used directly to monitor day-to-day developments during experimentation, and communicate findings to other laboratory personnel This was accomplished by generating on-screen graphs of data or by printing graphs and summary tables for circulation (see Fig 1B)

Storage Files

All storage files were of identical format (except for data and labels) so that they would each be compatible with RDIP and any Lotus templates used for displaying graphs The standardized worksheet allowed storage of exactly 1040 ANOVA cells containing 16 data points each, organized in 260, 4×16 storage blocks A factorial experiment consisting of 80 ANOVA cells could be stored for each of the 13 dependent measures, assuming one repeated measure (sampling periods) moving across rows The dependent measures were organized from left to right across the top of the worksheet and could be viewed 2 at a time for 16 subjects through a permanent window The left and right extremes of one storage file are shown in Fig 4 as they might appear after retrieval to the Lotus system The extreme right side of the storage file contained subject identification and was always visible in the right hand window as the user scrolled through each measure Subject groupings were arranged from top to bottom in the storage file The file in Fig 4 contained all data for mice aged 1–2 and 2–4 months, with test days and age variables arranged and labeled in the right window, from top to bottom in the file

Summarizing Data

By using a custom menu accessible from the storage file, summary statistics for any individual 4×16 cell block of the storage file could be calculated, and by combining the storage file with any of a set of additional customized graphics templates, pre-formatted graphs could be displayed or printed (see Fig 1B) As shown hypothetically in Fig 5, the template for displaying tables and graphs was of identical

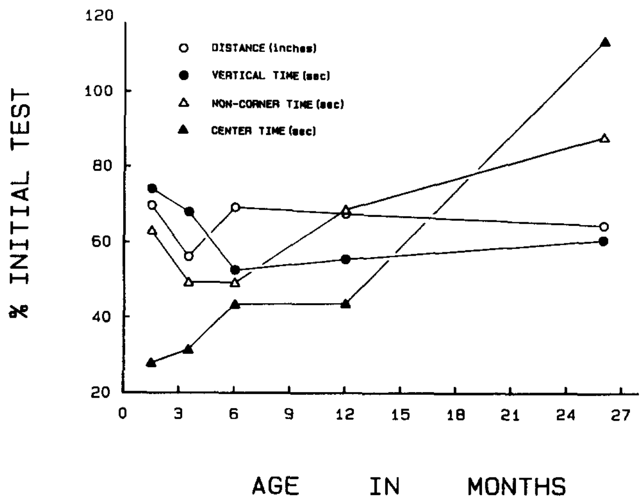

FIG 7 Summary graph of experimental results generated by a plotter and plotter graphics software The graph shows the effect of age upon mean values of each activity measure on test day 2, expressed as a percentage of that measure during the initial (day 1) test

format to the data storage file, with the exception that an additional area containing formulas appeared at the bottom of the file These formulas addressed blank cells in the template which corresponded to parallel cells containing data in the storage file The graphics template was retrieved from the fixed disk and the Lotus commands / *F*ile *C*ombine *C*opy *E*ntire file caused the data storage file to overlay the template The previously blank cells of the template where then occupied by data, allowing the formulas to calculate values Graphics templates, pre-set to display graphs of different formats, were permanently stored on the fixed disk and could be combined with any of the data storage files

Figure 6 shows a portion of the tables area from a graphics template which was combined with a data storage file Each number in the tables was the result displayed by a formula (shown at the bottom of Fig 6) which addressed one or more of the cells in the template above it For example, the data for total distance in 1–2 month mice on test day 1 were entered in columns E, F, G, and H (intervals 1–4), and rows 4 through 15 (subjects 1 through 12) The formula @SUM(E4 H15)/@COUNT(E4 E15) combined data for the 4, 5-min intervals and computed the mean session totals for the distance measure on day 1 The formulas below this one calculated the same values for tests 2, 3, and 4, and the adjacent row calculated days 5–8 (The file allowed for 8 test days, the empty cells returning a value of "ERR") The "space" menu option drew a line graph showing total distance as a function of test days 1–6, calculated from the values of these formulas (the "ERR" values were ignored) Each of the other menu options (Fig 6, top) displayed a new table and generated the corresponding graph Graphs of interest could be saved to disk and subsequently printed using the Lotus Printgraph utility, and tables could be saved as ASCII files and incorporated into reports generated with a word-processing program

ANALYSIS AND PRESENTATION

In the present study, formal data analysis was accomplished by retrieving data storage files, editing the data, and generating an ASCII data file of a format which would be accepted by Ganova, a general univariate and multivariate analysis of variance program (most other statistical packages will accept an identically structured file) The storage file format was such that any necessary restructuring of the data could be accomplished by simply re-arranging rectangular blocks of data within the Lotus system prior to creation of the ASCII file The analysis was then carried out within Ganova (see Fig 1C), which structures each analysis appropriately according to a series of user prompts Inspection of the data by the methods outlined above allowed identification of several variables of interest, and these measures were subjected to separate 5×4×6 analyses of variance with Test day and 5-minute periods as within-groups factors, and Age as a between groups factor

Presentation quality graphs were generated by creating ASCII files from Lotus tables which could be used by Sigmaplot, a plotter graphics program (see Fig 1D) which allowed on-screen editing and plotting of graphs Figure 7 is a sample graph plotted on glossy paper using Sigmaplot and the HP 7475A plotter This figure shows transcribed data for the purpose of summarizing the major findings in the study of C57BL/NNia mice The summary shows total distance, vertical time, non-corner time and center time during test 2 for each age group, expressed as a percentage of the respective means for each measure during the initial test (This measure approached 100% as the decrease between test 1 and 2 became less marked for a particular variable) Inspection and analysis of the 13 dependent measures using the process described above resulted in the isolation of two major variables, non-corner time and center time, which showed marked change with age in the rate at which they decreased as a function of test sessions (full discussion of these data are to be published elsewhere)

SUMMARY

The traditional task of transcribing, summarizing, and submitting data for mainframe computer analysis assumes impossible proportions in the context of apparatus which automatically generates 20 or more dependent measures, any of which may interest the experimenter This problem is acute in studies of age differences, which often require large experimental designs for proper interpretation The system described here addressed many of the problems of data management engendered by the use of such apparatus, by employing several commercially available software packages all running on the same microcomputer A simple descriptive study of age differences was used to illustrate how an experimenter could employ such software to peruse, extract, and present relevant information from the powerful database provided by multivariate activity measurement It is concluded that a commercially available spreadsheet/database management software package can be easily adapted for handling of large samples of multivariate activity data, and readily linked to software involved in the collection and analysis of data

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