in the region of the maximum activity is probably the most important contribution of this study. This positivity is a stimulus-related cochlear response that is confined to a limited spatial extent of the inner ear, and which is an independent response from the familiar CM and DIF-SP components which appear as voltages across the organ of Corti. The positive AVE-SP component is the polarization of an entire segment of the cochlea. Since the only electrical connection between the membranous cochlea and the rest of the body is through the internal auditory meatus, via the eighth nerve and blood vessels (*11*), it can be conjectured that the positive AVE component can serve as a hyperpolarizing electrical agent acting on the dendrites that originate in the region of maximum positivity. The source of this positive AVE response is not yet identified with certainty. This response is possibly due to a voltage drop caused by longitudinal current flow within the cochlea between regions of strong and weak excitation.

PETER DALLOS
Z. G. SCHOENY
M. A. CHEATHAM
Auditory Research Laboratory and
Department of Electrical Engineering,
Northwestern University,
Evanston, Illinois 60201

References and Notes

1. G. von Békésy, *J. Acoust. Soc. Amer.* **22**, 576 (1950); H. Davis, C. Fernández, D. R. McAuliffe, *Proc. Nat. Acad. Sci. U.S.* **36**, 580 (1950).
2. H. Davis, D. H. Deatherage, D. H. Eldredge, C. A. Smith, *Amer. J. Physiol.* **196**, 251 (1958).
3. H. Davis, C. Fernández, R. Goldstein, *Cold Spring Harbor Symp. Quant. Biol.* **17**, 143 (1952); J. R. Johnstone and B. M. Johnstone, *J. Acoust. Soc. Amer.* **40**, 1405 (1967); R. Kupperman, *Acta Oto-Laryngol.* **62**, 465 (1966); G. A. Misrahy, E. W. Shinaberger, K. M. Hildreth, *Wright Air Development Center Technical Report 45–467* (Wright-Patterson Air Force Base, Ohio, 1957), p. 1; P. E. Stopp and I. C. Whitfield, *J. Physiol.* **175**, 45P (1964); R. Butler, T. Konishi, C. Fernández, *Amer. J. Physiol.* **199**, 688 (1960).
4. T. Konishi and T. Yasuno, *J. Acoust. Soc. Amer.* **35**, 1448 (1963); V. Honrubia and P. Ward, *ibid.* **45**, 1443 (1969).
5. I. Tasaki, H. Davis, J. P. Legouix, *ibid.* **24**, 502 (1952).
6. P. Dallos, *ibid.* **45**, 999 (1969).
7. Under ideal recording conditions the DIF and AVE responses can be registered independently from one another. If the electrodes are well placed and if the electrical paths from them to the various sources of potential are symmetrical, then any change that might occur in the potential difference across the cochlear partition is manifested by the DIF response only. Conversely, under such conditions any overall shift in voltage level by a cochlear cross section would modify the AVE component alone. In practice the electrodes are never perfectly balanced, and consequently the recorded components are not completely independent. The errors resulting from a given electrode imbalance can be estimated, and thus one can guard against unwarranted use of the data. The electrode imbalance can be obtained, at least as a first approximation, from the comparison of the cochlear microphonic outputs of SV and ST electrodes at high frequencies (*6*). It is important to point out, however, that even when perfect a-c balance (that is, that for CM) exists between two electrodes, they are not, in general, "balanced" for SP. For example, in Fig. 1c the responses are shown from scalae tympani and vestibuli from the first turn at a high frequency. In this situation the CM's from the two electrodes are virtually identical in magnitude but opposite in phase; there is balance. Note, however, that the SP magnitudes are not the same; the SP from the ST is considerably greater than that from the SV. This indicates the presence of a "common-mode" d-c potential, the very item of interest in this communication that is labeled as the AVE component.
8. G. von Békésy, *J. Acoust. Soc. Amer.* **25**, 770 (1953); S. M. Khanna, R. E. Sears, J. Tonndorf, *ibid.* **43**, 1077 (1968).
9. I. C. Whitfield and H. Ross, *ibid.* **38**, 126 (1965); M. Engebretson and D. H. Eldredge, *ibid.* **44**, 548 (1968); H. Davis, *Ann. Otol. Rhin. Laryngol.* **77**, 644 (1968).
10. At first glance this contention might appear to be contradictory to the findings of I. Tasaki and C. Fernández [*J. Neurophysiol.* **15**, 497 (1952)] that the electrical spread in the cochlea from turn to turn is negligible. Actually there is no contradiction. Tasaki and Fernández obtained their attenuation figure of 6 db/mm from differential electrode recordings; in other words, this attenuation constant would apply for our DIF component. When not using differential electrodes, one observes much less attenuation of electrical potentials, probably of the order of 1 to 2 db/mm (*6*). This latter figure is applicable for the AVE component. Thus, it is quite reasonable to assume that the negative AVE component is a response that results from current spread from active remote regions. That this is so can be highlighted by the prominence of this response in regions and at frequencies where no local traveling wave activity exists, that is, in the higher cochlear turns at high frequencies.
11. G. von Békésy, *J. Acoust. Soc. Amer.* **23**, 18 (1951).
12. Supported by NIH grants.

4 August 1970

■

Intelligence Quotient Pattern over Age: Comparisons among Siblings and Parent-Child Pairs

Abstract. *Comparisons between sibling and parent-child pairs with unrelated control pairs matched for year of birth and parental education were made to determine the relative heritability of the general level of intelligence quotient as opposed to that of the sequential pattern of IQ change over age (3 to 12 years). There was greater similarity among related siblings relative to matched controls for general level than for pattern of IQ over age. Relationships between the IQ's of children and that of their parents as children were not consistent across age.*

A recurring question concerns the relative heritability of general IQ. One position is that IQ can be altered by certain environmental factors, such as programs of enrichment (*1*). The opposite position suggests that the genetic component of IQ is so significant that it is unrealistic to hope that enrichment programs will be able to change IQ very much, particularly for relatively normal children (*2*).

The issue is exemplified by two sets of apparently contradictory findings: (i) the IQ's of severely deprived youngsters can be raised by certain programs of stimulation and compensatory education (*1, 3*); but (ii) the correlation between the IQ scores of pairs of individuals increases dramatically and consistently with the degree of their genetic, as opposed to their environmental, relationship (*2, 4*).

Part of this controversy may be resolved by distinguishing between the *general level* of IQ as reflected in an IQ score assessed at a single age and the sequential *pattern* of IQ change that might occur over age. It is likely that many normal children display substantial changes in IQ during childhood and that these shifts over age constitute meaningful and reliable trends (*5*). Since much of the current emphasis on compensatory education programs is concerned with changing IQ, it would be valuable to determine if such patterns possess as much heritability as the general level of IQ.

Most of the evidence for the genetic basis of intelligence has been determined with single-age (or at least separate-age) correlations between genetically related individuals. These data demonstrate the heritability of the general level of IQ, but they do not demonstrate the heritability of IQ changes over age. Even if these methods suggest that the genetic contribution to the general level of IQ is substantial, meaningful changes in IQ over age are still possible (as produced by enrichment programs, for example).

In this paper I report an examination of the relative heritability of the general level of IQ as opposed to the pattern of IQ change over age. This issue was addressed by a comparison of the similarity of patterns of IQ change over age among siblings and among parent-child combinations with the similarity of patterns for unrelated subjects matched for year of birth and parental educational level. These comparisons were made first when both the general level of IQ and the pattern over age were allowed to operate and then when the general level was extracted and only the pattern of change over age was allowed to operate.

For the sibling comparisons, subjects were drawn from the Fels Longitudinal Study [see (*6*) for a description of the sample] in which tests of general intelligence had been administered (predominantly by the same examiner) every 6 months from 3 to 6 years of age, then every year through age 12. As a group, these children have above average intelligence (Binet mean of 117, varying somewhat with age) but average variability at any given age (standard deviation, $s = 16.9$).

Those children having at least one sibling in the Fels study and no more than two consecutive tests missing between 3 and 12 years of age were selected for analysis. Within this group all subjects were paired with each of their siblings (*7*) to produce 18 male-male pairs (13 families), 28 female-female pairs (19 families), and 54 male-female pairs (30 families).

An unrelated pair of subjects was matched with each sibling combination in the following manner. If *A* and *B* constituted a sibling pair, then the corresponding unrelated control pair, *A-C*, was determined such that *A* was arbitrarily chosen from the two choices of *A* and *B*, and *C* was unrelated to either *A* or *B* but matched with *B* with respect to sex, year of birth, and average parent educational level (midparent education level) on the basis of the seven-point educational scale of the Hollingshead two-factor index of social position. The *B* and *C* matches differed by an average of .59 parental education points ($s = .51$) and 15.89 months between birthdays ($s = 14.37$), and these figures were characteristic of each of the three sex groupings as well. The average difference in age between pairs was 52.9 months ($s = 42.6$) for siblings and 49.5 months ($s = 45.3$) for unrelated control pairs.

In order to eliminate general group trends in IQ over age and to permit the use of subjects who had been given a few IQ tests other than the Stanford-Binet test (*8*), standard scores were computed for each subject from the mean and standard deviation for all children in the Fels population on that test at that age (average $N = 151$). In order to minimize the influence of a particular test administration and to handle missing data (*8*), individual IQ curves were smoothed by the "moving mean" technique in which the scores at each set of three adjacent ages were averaged. Each subject then had 11 smoothed standardized IQ scores based upon his performance between 3 and 12 years of age.

Similarity in pattern of IQ change over age was assessed by the Cronbach and Gleser technique (*9*) of first taking the square root of the sum of squared deviations between corresponding points along these smoothed curves for any pair of subjects. Such a procedure allows differences in the general level of IQ (that is, overall mean IQ) to operate in addition to differences in the sequential pattern of IQ inflections over age. Thus, because sibling IQ's at a given age are known to correlate approximately .49 (*2, 4*), greater similarity should be observed for siblings than for unrelated children. In contrast, when each subject's smoothed scores are taken as deviations about his own mean of 11 values and then the square root of the sum of the squared deviations between corresponding points is computed for each pair of curves, the general level of IQ is eliminated and only fluctuations in pattern are reflected in such an index. If the pattern of IQ change over age, regardless of general level, has heritability, then siblings should be more similar than unrelated children on this measure as well.

The criteria for selecting parent-child pairs and the techniques of analysis of the resulting data were the same as those used for siblings. A total of 13 father-son (9 families), 11 mother-daughter (9 families), and 11 cross-sexed parent-child pairs (10 families) qualified for analysis. Each child was matched with a nonrelated subject from these groups on the basis of sex, year of birth, and midparent educational background. Thus, for each related parent-child combination, the control pair consisted of the same parent coupled with an unrelated child who was matched with the parent's own child. The mean parental educational difference between matched children was .58 ($s = .64$) points, and the mean age difference was 14.86 ($s = 8.96$) months.

The parent-child comparisons were between the IQ's of the *parent as a child* assessed between 3 and 12 years of age and the IQ's of their child assessed years later when the child was 3 to 12 years of age. As in the case for siblings, the pattern of same-age parent-child IQ's was compared for similarity with matched control pairs when the general level of IQ was allowed to operate and when only pattern over age exclusive of general level was involved.

Initial analyses of variance on the sibling data failed to indicate that the difference between related and unrelated pairs interacted with sex (interaction for three sex groups: $F = 1.63$, d.f. = 2/97; interaction for male versus female pairs only: $F = 2.47$, d.f. = 1/44). Consequently, the data were combined across sex grouping and are presented in Table 1. Sibling IQ's were more similar than matched unrelated controls when the general level of IQ was allowed to operate ($P < .0001$), a result that reflects the common finding that sibling IQ's correlate approximately .49 (*2, 4*). In contrast, when the general level of IQ was extracted, there was no more similarity in the pattern of inflections of IQ over age for siblings than for matched unrelated children (*10*).

Since the means and variances of the similarity scores were different when the general level was considered than when it was extracted, these two distributions were separately standardized and an analysis of variance was performed to determine if the difference in similarity between sibling and control pairs was greater when general level was operative than when it was not. The significant interaction ($F = 4.92$, d.f. = 1/99, $P = .03$) between related-unrelated groups and similarity measure implied that sibling similarity was greater for general level plus pattern than for the pattern of IQ change alone.

For the parent-child comparisons, neither analysis (with or without general level) revealed a significant effect and there was no significant difference between the two analyses. Although the number of parent-child pairs was fewer than the number of sibling pairs (35 versus 100), the difference in similarity scores when general level was operative between related and unrelated pairs was 2.7 times as large for siblings as for parent-child pairs. These parents and their children apparently do not evidence a great deal of similarity in general IQ level or in IQ pattern over age relative to matched unrelated controls.

The fact that parent-child pairs were not significantly more similar to one another than unrelated controls, even when the general level of IQ was operative (even though the data are in the predicted direction), seems to con-

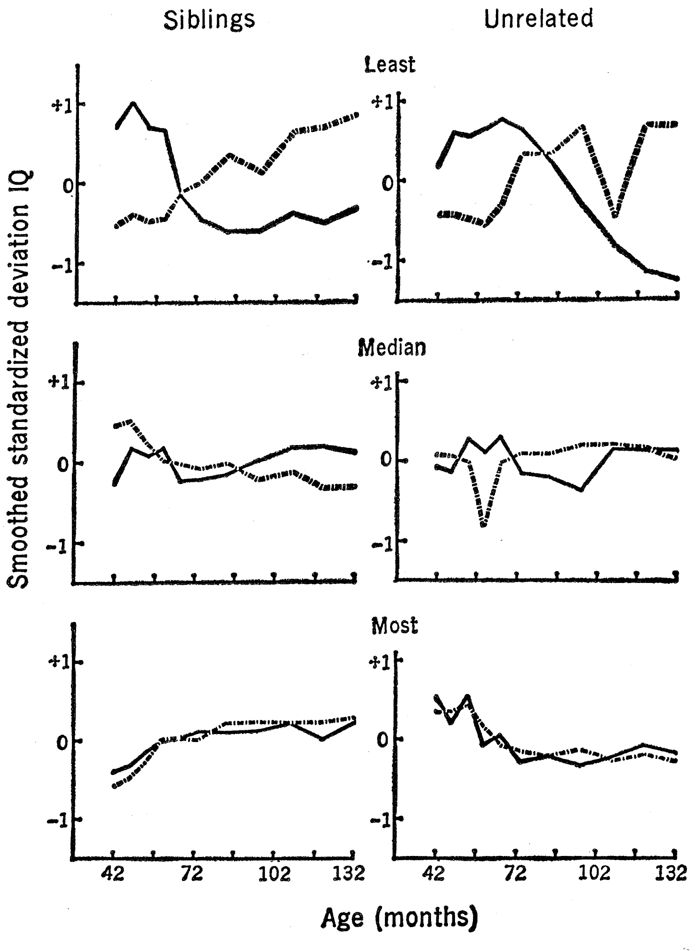
Table 1. Mean square root of the sum of squared deviations for sibling and parent-child groups.

Pairings	General level + pattern	Pattern alone
Siblings ($N = 100$)	2.23	1.27
Unrelated	3.04	1.40
t (P)	4.36 ($P < .0001$)	.98
Parent-child ($N = 35$)	2.91	1.43
Unrelated	3.22	1.47
t	.88	.31

tradict the well-known finding that the correlation between the IQ's of parents and their children is approximately .50 (*2*, *4*). However, this figure typically represents the correlation between adult parent and young child. In contrast, the analysis presented here is sensitive to parent-child similarity when the IQ's of both parent and child are measured at the same chronological age during development (that is, parent at age 3 correlated with his or her child at age 3). Table 2 presents the simple correlations between smoothed IQ at each age for the sibling and parent-child pairs used in the above analyses. The siblings show a constant correlation (r) over all ages, and the median coefficient of .55 is very close to the comparable figure of .49 reported by others (*2*, *4*). In contrast, the parent-child correlations were lower than those for siblings at each of the 11 ages examined, having a median $r = .29$ (*11*). This relatively low value may account for the failure in this study to obtain a significant degree of relative similarity between parents and their children even when general level was included, and is probably caused by the fact that there are many more years separating same-age assessments for parent-child than for sibling pairs.

The fact that siblings displayed greater similarity in general level of IQ than in the pattern of inflections over age might have been expected if IQ does not change very much during childhood. For example, if there were a precise level of mental performance for each individual which is constant over age, subtracting a subject's mean IQ from each of his scores might leave only a "pattern" of random error. One would not expect to find sibling or parent-child similarity in this unsystematic "error" variation over age. However, if it can be shown that substantial age trends in IQ do occur within individuals, then the IQ pattern over age exclusive of general level is not simply random variation and may represent important changes in mental ability.

The data presented above for sibling and parent-child pairs involved 136 subjects. The 11 scores for each individual were subjected to Ferguson's nonparametric trend analysis (*12*) to detect monotonic, bitonic, and tritonic IQ patterns. Eighty-nine of 136 individuals (65 percent) displayed a significant (.05 level) basic trend (49 monotonic, 19 bitonic, and 22 tritonic) in IQ over age. Although the 11 scores of any individual will correspond to some



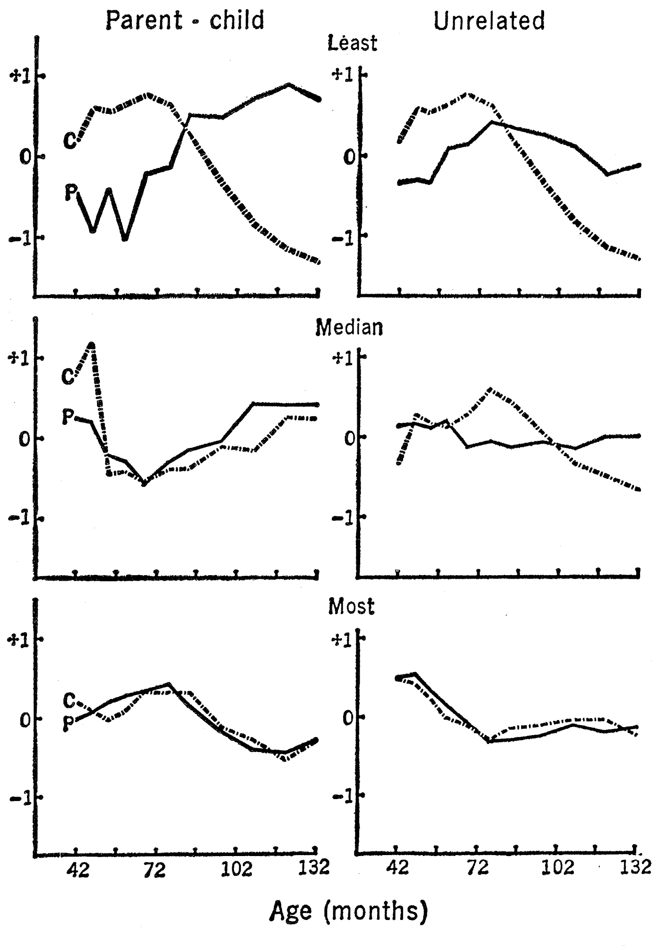


Fig. 1 (left). Trends in IQ for the least, median, and most similar sibling and control pairs. Fig. 2 (right). Trends in IQ for the least, median, and most similiar parent-child and control pairs. (*P*, parents; *C*, child).

Table 2. Correlations at different ages between smoothed IQ's for siblings and parent-child pair. Siblings: $P < .001$ for all r's; parent-child: $r_{.05} = .28$; $r_{.01} = .39$.

Pairings	Age at test administration (months)										
	42	48	54	60	66	74	84	96	108	120	132
Siblings ($N = 100$)	.54	.50	.51	.39	.52	.59	.63	.57	.57	.58	.55
Parent-child ($N = 35$)	.36	.29	.27	.19	.43	.45	.50	.35	.28	.21	.17

pattern (for example, the trivial case of a tenth degree polynomial), these data suggest that a rather large percentage of subjects display relatively simple (monotonic, bitonic, or tritonic) trends.

For the sibling analyses reported above, one member of 84 percent of the related pairs and both members of 46 percent of the pairs had significant trends as defined above. For the parent-child analyses, one member of 100 percent of the pairs and both members of 57 percent of the pairs had significant trends. Since there were no group trends because scores standardized (mean = 0; standard deviation = 1) on this sample within each age were employed, it is unlikely that these individual patterns represent a simple effect of repeated testing. Consequently, it would appear that removing the mean IQ does not leave a residual of mere random error in a sizable proportion of the pairings, and that the form of such IQ patterns over age does not appear to be shared by siblings or parents.

The following figures provide a notion of the extent of IQ change over age reflected in these patterns: the average individual range of smoothed standardized scores for each of the 136 subjects was .94 standard deviation units or approximately 16 IQ points (range of change: 5 to 36 IQ points). These figures are somewhat conservative since extreme values were minimized by the use of the smoothed scores which represent a mean of three IQ determinations (mean range of raw IQ scores = 24 points).

To illustrate the effects described above, Figs. 1 and 2 present the IQ trends for the least, median, and most related sibling, parent-child, and nonrelated control pairs. These are not matched pairs, but rather the median and extremes of each distribution, related and nonrelated. The graphs illustrate that sizable changes in IQ can occur over age and that trends of related individuals do not possess obviously greater similarity than those of unrelated pairs.

Figures 1 and 2 also illustrate in part that the inflections in the IQ patterns of siblings were not simply displaced from one another by the number of months separating the birthdays of the siblings. If pattern similarity were greater when same-year (contemporaneous rather than same-age) comparisons are considered, one would expect a negative correlation between the IQ dissimilarity score and the number of months separating the birthdays of the siblings. The correlations were nonsignificant and opposite in sign from this expectancy ($r = .11$ with general level; $r = .07$ without general level), which suggests that IQ patterns were not more similar for closely spaced than for widely spaced siblings. Visual inspection of the graphs by two independent observers also indicated that patterns did not appear to be more similar when siblings were matched at contemporaneous ages than when they were matched at the same chronological age.

Taken together, these data suggest that relatively simple trends in IQ over age occur in a large number of normal children. Furthermore, although the general level of IQ appears to show heritability, the pattern of IQ change over age possesses far less heritability (if any at all); a firm conclusion must be substantiated with larger samples and with pairs of individuals having greater genetic relationship (for example, twins).

Siblings (and parent-child pairs) share some environmental elements (for example, general atmosphere of intellectual encouragement) as well as genes in common. However, whatever the factors that determine IQ change over age, apparently they are not simply the general family intellectual climate available to each sibling. Rather, one might speculate that the salient variables are relatively more specific events and intellectual circumstances which quite possibly interact with age, personality, social, and motivational factors. Perhaps designers of enrichment programs might look to these areas when developing their curricula.

These results and those of others (*2*, *4*) suggest that the genetic heritage of middle-class normal children partially governs the general segment of the total IQ dimension within which an individual is likely to function. In contrast, other factors, not purely genetic in origin and possibly involving complex environmental-personality-social interactions, determine meaningful fluctuations in mental performance over age within that general range. Furthermore, these data illustrate that evidence for the genetic basis of a trait (such as intelligence), which is grounded in the correlation between genetically related individuals, does not necessarily imply that the trait is immutable to change. This statistical fact plus the observations that shifts in IQ (i) are often substantial, (ii) characterize a sizable proportion of normal children, and (iii) may not possess as much heritability as general level of IQ should be considered in discussions of the rationale and theoretical potential of enrichment programs.

ROBERT B. MCCALL
Department of Psychology,
Fels Research Institute,
Yellow Springs, Ohio 45387

References and Notes

1. J. McV. Hunt, *Intelligence and Experience* (Ronald, New York, 1961); *The Challenge of Incompetence and Poverty* (Univ. of Illinois Press, Urbana, 1969).
2. A. R. Jensen, *Harvard Educ. Rev.* **39**, 1 (1969).
3. M. Deutsch, I. Katz, A. R. Jensen, Eds., *Social Class, Race, and Psychological Development* (Holt, Rinehart, & Winston, New York, 1968); S. W. Gray and J. O. Miller, *Rev. Educ. Res.* **37**, 425 (1967); J. Hellmuth, Ed., *Disadvantaged Child* (Brunner/Mazel, New York, 1968), vol. 2.
4. L. Erlenmeyer-Kimling and L. F. Jarvik, *Science* **142**, 1477 (1963).
5. L. W. Sontag, C. T. Baker, V. L. Nelson, *Monogr. Soc. Res. Child Develop.* **23**, No. 68 (1958).
6. See Sontag *et al.* (*5*), pp. 15–18, for a description of this sample.
7. When more than three siblings from one family were involved in any single sex grouping, one pairing was randomly dropped from the analysis in order to eliminate this lack of independence.
8. Ninety percent of the tests given the siblings, 83 percent of the tests on parents, and 77 percent of the tests on their children were Binet assessments. The Merrill-Palmer (4 percent for siblings, 17 percent for parents) and the Wechsler Intelligence Scale for Children (6 percent for siblings and 23 percent for children of parents) were the other two tests employed. In 93 percent of the pairs in the entire study, each member of the pair had 8 or more of the 13 possible IQ assessments.

→ L. J. Cronbach and G. C. Gleser, *Psychol. Bull.* **50**, 456 (1953); E. F. Heermann, *ibid.* **63**, 128 (1965); J. E. Overall, *ibid.* **61**, 195 (1964).

10. Sontag *et al.* (*5*) reported that similarity in IQ change over age increased with increased genetic relationship between the members of the pairs. Their procedure permitted general level to operate and did not reflect pattern over age alone. Thus, their results are in accord with the data presented here. Furthermore, the analyses reported here were also performed on IQ's taken between 36 and 66 months of age and separately on IQ's determined between 72 and 144 months of age, since shifts in IQ are often found at approximately 6 years. The results for these two age periods were identical (sibling similarity with general level included, $P < .001$, but no

difference when pattern alone was considered).

11. The median correlation of .29 between the IQ's of same-aged parents and their children is somewhat lower than the figure of .56 reported for the same kind of comparison by C. Burt [*Brit. J. Psychol.* **57**, 137 (1966)] and E. W. Reed and S. C. Reed [*Mental Retardation: A Family Study* (Saunders, Philadelphia, 1965)]. The age of the subjects at testing is not clear in Burt's report but testing occurred during their early school years (as was true for Reed and Reed), an age when the coefficients presented in this report are highest. In the data presented here the low parent-child correlations relative to those for siblings may derive from the fact that more non–Stanford-Binet assessments were present in the parent-child than in the sibling protocols.
12. G. A. Ferguson, *Nonparametric Trend Analysis* (McGill Univ. Press, Montreal, 1965).
13. This research was made possible by more than 40 years of effort by the staff of the Fels Research Institute, L. W. Sontag, Director; by the continuous support of the Fels Fund of Philadelphia; and by PHS grants FR-05537, HD-00868, and FR-00222 to the Fels Research Institute and HD-04160 to R.B.M. I thank R. Q. Bell, V. Crandall, D. Eichorn, N. Hurlburt, A. R. Jensen, A. Kagan, J. I. Lacey, R. M. Liebert, J. C. Loehlin, N. Robinson, H. B. Robinson, and L. W. Sontag for their helpful comments on earlier drafts of this report and L. Christensen, K. Pryor, J. Peterson, and P. Savoy for their preparation of the data and manuscript.

8 July 1970; 25 August 1970 ■

Neuromuscular Synapse: Stochastic Properties of Spontaneous Release of Transmitter

Abstract. *The spontaneous quantal release of transmitter from the motor nerve endings is a random process which follows the Poisson theorem; the liberation of each quantum is independent of the release of previous quanta. Increase in the extracellular calcium concentration produces a statistical interdependence in the release of the spontaneously appearing packages.*

Transmitter is liberated at the neuromuscular junction and at neuronal synapses as multimolecular packages or quanta (*1*). There are two main factors that determine the rate of appearance of these quanta: (i) the membrane potential of the presynaptic terminal (*2*) and (ii) the calcium ion concentration in the external medium (*3*). When an action potential reaches the motor nerve endings, several hundred quanta are released within a millisecond giving rise to an end plate potential (EPP), and thus transfer of the electrical information across the neuromuscular synapse is obtained. At rest, the rate of liberation is approximately one quantum per second. Our report deals with some of the statistical features of these spontaneously occurring quanta and with the effect of calcium ions on them (*4*).

The experiments were performed in vitro on the sartorius neuromuscular preparation of the frog *Rana ridibunda*. Conventional methods of intracellular recording were employed (*5*). The spontaneous activity (miniature end plate potential-MEPP) was first recorded in normal ionic environment (standard Ringer solution composition: 116 m*M* NaCl, 2.0 m*M* KCl, and 1.8 m*M* $CaCl_2$). The results (Table 1) show that the discharge is random in nature and fits the Poisson theorem (*6*). Thereafter, while the microelectrode was still lodged in the same fiber, the calcium concentration of the medium was elevated to 15 mmole/liter [by isotonic substitution for NaCl; the resulting decrease in sodium concentration has a very little effect on transmitter release (*7*)], and a second series of records was taken. Under this condition the discharge of the MEPP's no longer fits the Poisson theorem (Table 1). Taking the chi-square test (*8*) as a measure of the agreement between the experimental results and the values predicted by the Poisson theorem, one can see that there is a profound change in the pattern of MEPP's brought about by elevating the extracellular concentration of calcium; the χ^2 for 1.8 m*M* Ca^{2+} is 1.6, showing a fair fit between the experimental and predicted values; the χ^2 for 15 m*M* Ca^{2+} is 56424, demonstrating the extreme poor fit to the Poisson distribution. Similar changes in the pattern of spontaneous release were obtained in ten additional experiments. The observed change in the pattern of release was reversible.

Table 1. Fit of MEPP appearance to Poisson distribution at normal and high calcium. The expected values were derived from the equation $N_x = N_T e^{-\alpha} \cdot \alpha^x / x!$ where N_T is the total number of samples, N_x is the number of samples containing x number of MEPP's, and α is the mean number of MEPP's in a sample. For normal concentration of calcium, α equals 0.0255, and for high concentrations of calcium α equals 0.0956. Each sample is a 20-msec period. The total number of MEPP's for the normal calcium concentration is 1187; for the high calcium concentration it is 998.

MEPP in sample (x)	N_x	
	Observed	Expected
Normal calcium concentration (1.8 mmole/liter)		
0	45388	45393.02
1	1167	1157.07
2	10	14.77
3	0	0.12
High calcium concentration (15.0 mmole/liter)		
0	9601	9486.40
1	735	906.64
2	65	43.53
3	21	1.39
4	10	0.03
5	6	0.00064

The stochastic features of the spontaneous release were further analyzed by the autocorrelation method. If the intervals between successive MEPP's are independent of one another, one would expect to obtain no correlation in a long series of intervals. However, if the appearance on one MEPP facilitates the appearance of the next MEPP or if a common cause increases the basis frequency of MEPP's occasionally, then a positive correlation among the intervals is expected. On the other hand, if the appearance of one MEPP inhibits the appearance of the next, a negative correlation is expected. In practice, the analysis of the experimental results was carried out as follows: first, the mean frequency of the MEPP's ($\bar{f}$) was calculated; then the frequency of the MEPP's in a given time interval after each event (f_t) was estimated by the autocorrelation method. For a process of independent release one would expect that the relative frequency, given by the ratio ($f_t/\bar{f}$) is unity for all time intervals. If a release of a quantum facilitates the appearance of the next quantum, the relative frequency will be greater than one, whereas if the release of a quantum inhibits the appearance of the next one, the relative frequency will be less than one. Figure 1A shows that under normal conditions (standard Ringer solution, 1.8 m*M* Ca^{2+}), the spontaneous release of transmitter is an independent process in the statistical sense; the appearance of a MEPP does not affect at all the probability of release of the successive quantum. At high external concentrations of calcium, the statistical behavior of the discharge is completely different; the relative frequency is significantly different from one (Fig. 1B). For example, in the 20-msec period after any given MEPP the probability of release is about five times larger than the basic probability. This enhanced probability of release decays slowly and reaches the basic value only after several seconds. The statistical interdependence between successive events explains the departure from a Poissonian process demonstrated in Table 1; if the probability of occurrence of a MEPP is