10. P. D. Eimas and J. L. Miller, *Science* **209**, 1140 (1980).
11. The terms "relational" and "nonlinear fashion" are ones recently adopted by Eimas and Miller (*10*) to describe perceptual compensation for context-conditioned variation in the speech signal, that is, shifts in the perceptual boundary that occur with changes in speaking rate [compare (*8*)]. Although they do not state it explicitly, Eimas and Miller (*10*) seem to imply that infants are responding to changes in speaking rates.
12. Both studies assumed that Miller and Liberman's demonstration (*8*) that the internal structure of the syllable and not just its overall duration affected the perceptual boundary for formant transition duration was sufficient to rule out a psychophysical account. Neither study considered the possibility that nonspeech sounds displaying similar internal relationships might give the same result.
13. P. K. Kuhl and J. D. Miller, *Science* **190**, 69 (1975); *J. Acoust. Soc. Am.* **63**, 905 (1978), K. N. Stevens, in *Human Communication: A Unified View*, E. E. David, Jr., and P. B. Denes, Eds. (McGraw-Hill, New York, 1972).
14. T. D. Carrell, D. B. Pisoni, and S. J. Gans [paper presented at the 100th meeting of the Acoustical Society of America, Los Angeles, 19 November 1980] found that the internal structure of the stimuli affected the location of the perceptual boundary in the way described by Miller and Liberman (*8*). Hence, these effects with nonspeech sounds depend on internal stimulus structure as well as overall duration.
15. This possibility seems unlikely since Carrell *et al.* (*14*) gave their subjects a questionnaire after the test, the results of which gave no indication that subjects perceived the stimuli as being speech or speechlike.
16. Information about the way infants discriminate these sounds is needed to test whether specialized speech processing capacities are responsible for context effects, because although the studies with adults have examined both discrimination and identification, Eimas and Miller (*10*), studying infants, tested only discrimination. As is the practice, the adult identification data provide a basis for designating which stimulus pairings involve between-category discriminations and which involve within-category ones. Hence, any adequate explanation for the underlying basis of context effects must account for the infant's performance along with that of the adult.
17. Each complex tone stimulus was composed of three sinusoids whose frequencies, amplitudes, and temporal characteristics matched those of a synthetic speech continuum between /ba/ and /wa/. Carrell *et al.* (*14*) provide a complete description.
18. Of the 100 infants who completed the experiment, approximately half were males and half females. A total of 262 infants were tested. Of the infants who failed to complete the experiment, 107 infants cried, 26 fell asleep, 24 rejected the nipple, and 6 were dismissed because of equipment failure or experimenter error. There was no statistically significant difference in dropout rate across any of the conditions.
19. In a recent replication of their earlier study J. L. Miller and P. D. Eimas [*Cognition* **13**, 135 (1983)] reported that subjects in the within-category conditions showed higher postshift rates of responding than control subjects did. Analysis of our data for the full 4-minute period after shift revealed a similar tendency in the performance of the within-category groups 35–55S and 15–35L. This indicates that the same underlying perceptual mechanisms are operating for both speech and nonspeech.
20. Indeed, R. Goldhor's recent model [*J. Acoust. Soc. Am.* **73**, S4 (1983)] of speech processing by the peripheral auditory system can account for the relational effects observed when syllable durations are increased. The same relational patterns are predicted without any assumptions about computation of speaking rate.
21. R. N. Aslin and D. B. Pisoni, in *Child Phonology: Perception and Production*, G. H. Yeni-Komshian, J. Kavanagh, C. A. Ferguson, Eds. (Academic Press, New York, 1980).
22. Supported by National Institute of Child Health and Human Development grants HD-15795-02 to P.W.J. and HD-11915 to R. N. Aslin and D.B.P. and by National Institute of Mental Health grant MH-24027 to D.B.P. We thank L. Kennedy and K. Kilborn for their assistance in testing infants and M. Posner, A. C. Walley, R. N. Aslin, and H. C. Nusbaum for helpful comments and suggestions on an earlier draft of this report.

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Fast Extracellular Calcium Transients: Involvement in Epileptic Processes

Abstract. *Improved liquid ion-exchanger microelectrodes made possible the observation of large, rapid decreases in the concentration of extracellular calcium ions during single epileptic spikes. Moreover, in definite cortical layers the decreases regularly started shortly before the onset of each epileptic spike. In view of the prominent role played by extracellular calcium ions in neuronal processes, including transmitter release and membrane excitability, these alterations probably exert a profound influence on the cellular events underlying epileptiform activity.*

Periods of synchronous neuronal activity are associated with substantial alterations in extracellular ion concentrations. It has been thought that these changes are rather slow, with time scales of hundreds of milliseconds, and that the participation of large populations of neurons is required. Such slow changes have been shown to occur in a variety of situations (*1*); however, it is important to determine whether rapid changes in extracellular ion concentrations take place during synchronous activation of groups of neurons, as during single epileptic events; these changes could then contribute significantly to the mechanisms by which synchronization occurs and hyperexcitability spreads. Technical limitations of liquid ion-exchanger electrodes, such as the slow rise time of responses, have prevented recordings of any rapid variations in the concentration of extracellular ions, especially variations in Ca^{2+}. Since ion-selective electrodes with short response rise times could be manufactured in our laboratory, we attempted to determine whether fast, transient changes in Ca^{2+} occur in epileptiform penicillin foci in the rat.

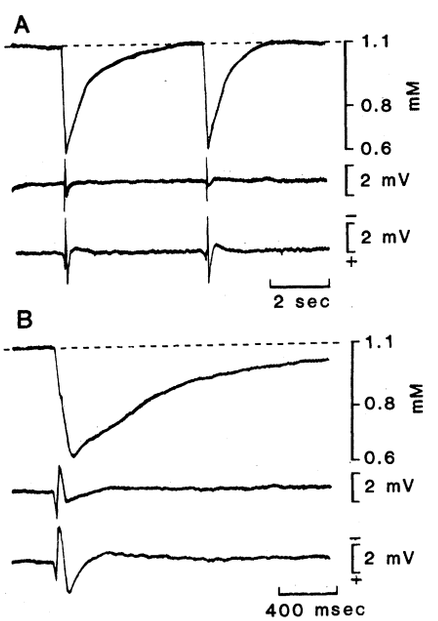

Fig. 1. (A and B) Alterations in the concentration of extracellular Ca^{2+} during spontaneous epileptic spikes in neocortical penicillin foci in rats. Upper traces, recordings of extracellular Ca^{2+}; middle traces, local field potentials (d-c–coupled) recorded through the reference side of the ion-sensitive microelectrode; bottom traces, electrocorticograms (a-c–coupled) from the neighboring cortical surface. The traces in (A) and (B) were obtained at two different sweep speeds. Recording depth was 600 μm below the cortical surface.

Ion-selective electrodes with a short response rise time were produced by the method of Ujec *et al.* (*2*). Conventional double-barreled ion-sensitive reference electrodes were siliconized and filled. A thinner, separately pulled micropipette was inserted into the ion-sensitive side until the longitudinal distance between the inner and outer tip was 5 to 10 μm, reducing considerably the longitudinal resistance of the ion-sensitive channel. The electrodes responded with an average of 26.93 ± 1.42 mV to a tenfold change in the Ca^{2+} concentration. The response rise time was measured in normal Ringer solution streaming in a thin tube. To eliminate electrical and mechanical artifacts, small amounts of a solution containing various Ca^{2+} concentrations were pressure-injected close to the tip of the electrode. Using a neutral ion exchanger (*3*), we measured the time to peak or trough of the responses at 2 to 4 msec. Recordings were performed in penicillin-induced cortical foci in rats under light halothane N_2O-O_2 anesthesia. Standard techniques were used for electrocardiographic recordings, for epicortical or forepaw stimulations, and for the creation of a restricted penicillin focus (20 IU of sodium penicillin G) in the forepaw area of the somatosensory cortex.

The average resting level of Ca^{2+} was 1.2 to 1.3 m*M*. After penicillin application, a progressive decrease of 0.1 to 0.2 m*M* could often be observed over a period of 2 to 4 minutes (*4*); then the resting level stabilized and remained constant throughout the experiments. During interictal discharges, extracellular Ca^{2+} levels decreased abruptly from baseline to minimum values of 0.45 to 0.55 m*M*, depending on the amount of time between penicillin application and

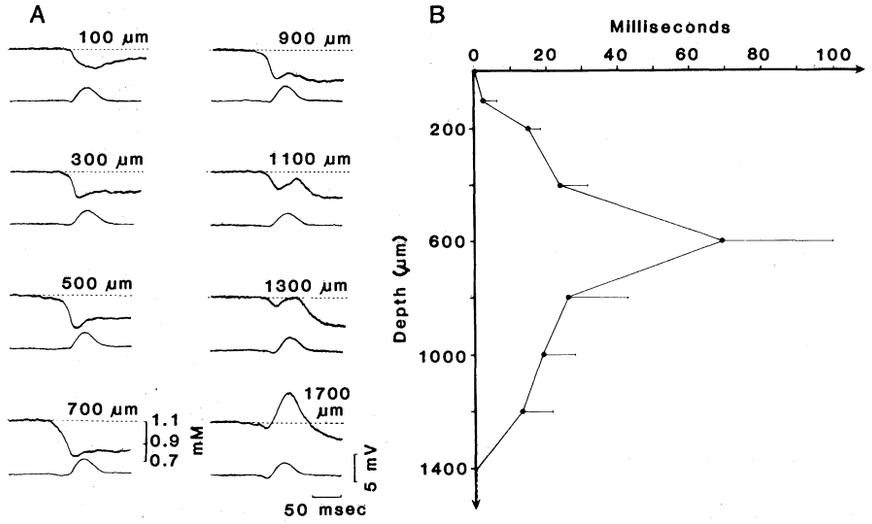

Fig. 2. (A) Laminar analysis of changes in extracellular Ca^{2+} and local field potentials recorded from different depths in cortical gray matter during spontaneous epileptic spikes. Upper traces, changes in Ca^{2+}; bottom traces, field potential recordings (d-c–coupled); negativity up. Depth of recordings is indicated above each trace. Baseline extracellular Ca^{2+} is 1.1 m*M* for each frame. (B) Delays between onset of changes in extracellular Ca^{2+} and onset of the corresponding field potential versus depth below cortical surface during spontaneous epileptic spikes. Each point represents the mean for eight experiments and each bar the corresponding standard error multiplied by 2.

recording and on the recording depth. Typical recordings are shown in Fig. 1. The shortest time to trough response was 38 msec for signals of 0.55 m*M* at recording depths of 600 μm. The steepest slope measured near baseline was 19.4 mmole/sec. In many recordings a hump was seen in the descending limb of the Ca^{2+} signal. Similar decreases were observed during epileptic spikes triggered by sensory or by direct cortical stimulations. The concentration of extracellular Ca^{2+} returned to baseline in 2.5 to 4 seconds, without, in most cases, any summation of Ca^{2+} decreases between successive spontaneous epileptic spikes (Fig. 1A).

The amplitude and shape of the extracellular Ca^{2+} signals were dependent on recording depth (Fig. 2A). At the surface no Ca^{2+} signal could be detected during paroxysmal field potentials. When the electrode was lowered 50 μm, Ca^{2+} signals could be observed. The largest reductions were seen at depths of 500 to 700 μm (Fig. 2A). At deeper recording sites the amplitude and abruptness of the signal diminished and the hump on the descending limb became prominent, so that there remained only an initial increase followed by a late, small decrease (Fig. 2A).

At depths at which the decreases in Ca^{2+} were largest, and provided the microelectrode was located in the center of the focus, the decreases preceded the local field potentials and an inflection point was apparent on the descending limb of the Ca^{2+} signal, the fall rate being smaller before the onset of the field potential and larger during it (Fig. 2). The latency between onset of the Ca^{2+} signal and onset of the field potential was largest (90 to 100 msec) at depths of 500 to 700 μm, with a certain variability for consecutive epileptic spikes (Fig. 2B). Above and below these depths the latency was smaller and could no longer be detected below 1400 μm (Fig. 2B). Similar latencies were also observed for epileptic spikes triggered by sensory or direct cortical stimulations.

These data show that large and very fast decreases in Ca^{2+} occur during a single epileptic spike. In view of the diffusion speed of Ca^{2+} in the extracellular space (*5*), the changes must reflect local events around the tip of the microelectrode, even though similar changes occur in the entire volume of cortex involved in the focus. Since glial cells are probably not responsible for such rapid changes (*6*), these decreases may reflect entry of Ca^{2+} into neuronal elements.

The respective contributions of pre- and postsynaptic Ca^{2+} entry to the extracellular Ca^{2+} decreases are not known, although experiments with the neurotoxin tetrodotoxin, which blocks action potential generation and thus synaptic transfer, suggest that, during paroxysmal events, a large amount of Ca^{2+} leaves the extracellular space through postsynaptic sites. This is further supported by the observation that, during ionophoretic release of excitatory amino acids, large decreases in extracellular Ca^{2+} occur which are not altered in the presence of tetrodotoxin (*7*).

In penicillin foci any paroxysmal field potential is invariably associated with intracellularly recorded paroxysmal depolarization shifts (PDS's) (*8*), which usually last 80 to 100 msec. At the postsynaptic level an inward, voltage-dependent Ca^{2+} current probably contributes to the envelope of depolarization of PDS's. Such conductances have been shown to be present in neocortical neurons (*9, 10*), and orthodromically evoked dendritic bursts in pyramidal neurons of penicillin-treated hippocampal slices are generated by such Ca^{2+} currents (*11*). Many of the decreases in Ca^{2+} are thus probably due to Ca^{2+} entry into postsynaptic membranes during PDS's. In addition, the lowering of extracellular Ca^{2+}, resulting in a reduced transmitter release, could limit the duration of synchronized activity. Indeed, the maximum Ca^{2+} decreases should coincide with the cessation of PDS's.

Of particular significance is the finding that, in definite cortical layers, Ca^{2+} decreases precede the onset of spontaneous or triggered epileptogenic field potentials (Fig. 2B). This observation may help to explain the triggering mechanisms of synchronous paroxysmal events: it has been proposed that reverberation of activity in recurrent excitatory pathways can account for the generation of such events (*12*). Thus, Ca^{2+} decreases before the onset of paroxysmal field potentials may be the result of the reverberating activity, which should then be restricted to terminals located in layer III and the border of layer IV. An alternative explanation is that the trigger mechanism is due to the activation of a distinct subpopulation of neurons with specific membrane properties that could synaptically drive the other cortical neurons. The decrease in Ca^{2+} before the onset of the paroxysmal field potential would then reflect the building up of activity in this subpopulation of neurons. This hypothesis is further strengthened by two recent studies. Connors *et al.* (*10*) showed in neocortical slices that neurons with bursting capabilities, and thus probably having dendritic Ca^{2+} conductances, are located in a narrow range of depths composing layer IV and the superficial part of layer V. Lockton and Holmes (*13*) found that the region most sensitive to penicillin in rat somatosensory cortex is located in laminae III and IV.

The rate of recovery of Ca^{2+} concentrations from trough levels is high when compared to the rate observed after decreases induced by excitatory amino acids (*14*). In view of the diffusion speed of Ca^{2+} in the extracellular space (*5*), this recovery rate cannot be explained solely by the migration of Ca^{2+} from zones surrounding the epileptogenic focus. Additional mechanisms must participate in the recovery, perhaps including active Ca^{2+} extrusion from cellular elements (*15*) or transition from bound to free Ca^{2+} in the extracellular matrix.

The humps often observed on the descending limb of Ca^{2+} recordings and the Ca^{2+} increases regularly detected in deep cortical layers during paroxysmal field potentials cannot be explained by a defective subtraction of the field potential from the signal of the ion-sensitive side: at the cortical surface full-sized field potentials were often recorded with no detectable signal on the Ca^{2+} recording. Moreover, in control experiments at various cortical depths in which artificial field potentials were delivered by stimulating electrodes, no appreciable artifact due to a defective subtraction was seen. Increases in extracellular Ca^{2+} have been observed during seizures (*4, 16*), particularly in deep layers (*17*). Several mechanisms may account for such a process, among which a shrinkage of the extracellular space due to osmotic imbalance is the most likely (*17*).

R. PUMAIN
I. KURCEWICZ
J. LOUVEL

Institut National de la Santé et de la Recherche Médicale, 2ter Rue d'Alésia, F-75014 Paris, France

References and Notes

1. C. Benninger, J. Kadis, D. A. Prince, *Brain Res.* **187**, 165 (1980); U. Heinemann, H. D. Lux, M. J. Gutnick, in *Abnormal Neuronal Discharges*, N. Chalazonitis and M. Boisson, Eds. (Raven, New York, 1978), p. 329; K. Krnjevic, M. E. Morris, R. J. Reiffenstein, *Can. J. Physiol. Pharmacol.* **58**, 579 (1980); C. Nicholson, *Dynamics of the Brain Cell Microenvironment* (MIT Press, Cambridge, Mass., 1980), p. 322; ———, G. T. Bruggencate, H. Stockle, R. Steinberg, *J. Neurophysiol.* **41**, 1026 (1978).
2. E. Ujec, O. Keller, N. Kriz, V. Pavlik, J. Machek, *J. Electroanal. Chem.* **116**, 363 (1980).
3. M. Oehme, M. Kessler, W. Simon, *Chimia* **30**, 204 (1976).
4. G. G. Somjen, *J. Neurophysiol.* **44**, 617 (1980).
5. R. Dingledine and G. Somjen, *Brain Res.* **207**, 218 (1981); M. E. Morris and K. Krnjevic, *Can. J. Physiol. Pharmacol.* **59**, 1022 (1981); C. Nicholson, *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **39**, 1519 (1980).
6. J. S. Kelly, K. Krnjevic, G. Somjen, *J. Neurobiol.* **2**, 197 (1969).
7. U. Heinemann and R. Pumain, *Neurosci. Lett.* **21**, 87 (1981).
8. H. Matsumoto and C. Ajmone-marsan, *Exp. Neurol.* **9**, 286 (1964); H. Matsumoto, G. F. Ayala, R. J. Gumnit, *J. Neurophysiol.* **32**, 688 (1969); M. Dichter and W. A. Spencer, *ibid.*, p. 663; D. A. Prince, *Exp. Neurol.* **21**, 467 (1968).
9. U. Heinemann and R. Pumain, *Exp. Brain Res.* **40**, 247 (1980).
10. B. W. Connors, M. J. Gutnick, D. A. Prince, *J. Neurophysiol.* **48**, 1302 (1982).
11. P. A. Schwartzkroin and M. Slawsky, *Brain Res.* **135**, 157 (1977); R. K. S. Wong and D. A. Prince, *Science* **204**, 1228 (1979).
12. G. F. Ayala, M. Dichter, R. J. Gumnit, H. Matsumoto, W. A. Spencer, *Brain Res.* **52**, 1 (1973); R. D. Traub and R. K. S. Wong, *Science* **216**, 745 (1982).
13. J. W. Lockton and O. Holmes, *Brain Res.* **190**, 301 (1980).
14. R. Pumain and U. Heinemann, *Adv. Biochem. Psychopharmacol.* **29**, 53 (1981).
15. P. F. Baker and H. Reuter, *Calcium Movement in Excitable Cells* (Pergamon, Elmsford, N.Y., 1975), p. 102.
16. J. Janus, E. J. Speckmann, A. Lehmenkuhler, C. E. Elger, in *Epilepsy and Motor System*, E. J. Speckmann and C. E. Elger, Eds. (Urban & Schwarzenberg, Baltimore, 1983), p. 259; E. Labeyrie and Y. Koechlin, *J. Neurosci. Methods* **1**, 35 (1979).
17. I. Dietzel, U. Heinemann, G. Hofmeier, H. D. Lux, in *Physiology and Pharmacology of Epileptogenic Phenomena*, M. R. Klee, H. D. Lux, E. J. Speckmann, Eds. (Raven, New York, 1982), p. 5.
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Detection of Intermodal Numerical Correspondences by Human Infants

Abstract. *Infants prefer to look at an array of objects that corresponds in number to a sequence of sounds. In doing so, infants disregard the modality (visual or auditory) and type (object or event) of items presented. This finding indicates that infants possess a mechanism that enables them to obtain information about number.*

Before children go to school they exhibit knowledge of enumerative procedures such as counting, of numerical relationships such as equivalence, and of arithmetic operations such as addition (*1*). These observations suggest that early mathematical knowledge develops from an innate base. Here we present evidence that 7-month-old infants match the number of objects in a spatial display to the number of sounds in a temporal sequence. These findings indicate that infants can detect numerical information and that they do so by use of a mechanism that is not limited to a single modality of sensation.

Human infants discriminate among visible displays of two, three, or four dots of white light (*2*) and between pictures of two or three objects varying in color, shape, size, texture, and arrangement (*3*). Although suggestive, these experiments do not reveal whether the basis of the discrimination is numerical information as such or specific visual patterns (*4*). We have now addressed this issue by investigating whether infants could detect numerical correspondences between sets of visible items and sets of audible items.

The experiments used a preferential looking procedure adapted from studies

Table 1. Attention to and preferences for numerically corresponding displays.

Experiment	Trial block	Duration of attention (seconds)		Preference for corresponding display		
		Corresponding display	Noncorresponding display	Proportion of duration†	Proportion of subjects‡	Subjects (*N*)
1	1	2.11 ± 0.89	1.99 ± 0.81	0.51	0.44	7
	2	2.02 ± 0.99	1.51 ± 0.79	0.58***	0.75**	12
	1 + 2	2.06 ± 0.71	1.75 ± 0.73	0.55**	0.75**	12
2	1	2.93 ± 1.09	2.91 ± 0.84	0.50	0.50	4
	2	2.74 ± 1.38	1.92 ± 0.91	0.58***	1.00***	8
	1 + 2	2.84 ± 1.23	2.42 ± 0.57	0.54**	0.75	6
3	1	3.03 ± 0.81	2.59 ± 1.02	0.54	0.56	9
	2	2.64 ± 0.95	2.32 ± 1.06	0.54	0.56	9
	1 + 2	2.84 ± 0.77	2.46 ± 0.80	0.54***	0.75*	12
1 + 2 + 3	1	2.64 ± 0.98	2.41 ± 0.96	0.52	0.50	20
	2	2.41 ± 1.09	1.92 ± 0.98	0.57***	0.72***	29
	1 + 2	2.53 ± 0.92	2.17 ± 0.79	0.54***	0.75***	30

†$P_d = D_c/(D_c + D_n)$, where P_d is the mean proportion of duration averaged over trials. and D_c and D_n are the mean durations of attention averaged over the sets of corresponding displays (c) and noncorresponding displays (n). This proportion was compared with that expected by chance, 0.50; significance was assessed by one-tailed *t*-tests with 15 degrees of freedom (d.f.) (experiments 1 and 3), 7 d.f. (experiment 2), or 39 d.f. (overall). ‡$P_s = S_c/(S_c + S_n)$, where P_s is the proportion of subjects, and S_c and S_n are the numbers of subjects whose mean proportion of duration was greater on the corresponding displays (c) or the noncorresponding displays (n); significance was assessed by one-tailed sign tests. *$P < 0.05$. **$P < 0.025$. ***$P < 0.01$.