than coughs and tones (for example, buzzes) may be used to produce the illusion. But, when a speech sound was deleted and not replaced with an extraneous sound, the gap was recognized in its proper location, and illusory perception of the missing sound did not occur. Of course, unlike extraneous sounds, a silence would not occur normally unless produced by the speaker. Also, silent intervals have functions akin to phonemes, requiring their accurate identification and localization for speech comprehension.

The ability to understand speech with masked phonemes is not surprising; the redundancy of language can account readily for this. However, our lack of awareness of restorative processes—our illusory perception of the speaker's utterance rather than the stimulus actually reaching our ears—reflects characteristics of speech perception which may help us understand the perceptual mechanisms underlying verbal organization.

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References and Notes

1. P. Ladefoged and D. E. Broadbent, *Quart. J. Exp. Psychol.* **12**, 162 (1960); T. G. Bever, J. R. Lackner, R. Kirk, *Percept. Psychophys.* **5**, 225 (1969).
2. R. M. Warren, C. J. Obusek, R. M. Farmer, R. P. Warren, *Science* **164**, 586 (1969).
3. G. Sherman, unpublished study.
4. Supported by PHS grant NB05998-03 and by the University of Wisconsin-Milwaukee Graduate School. I thank C. J. Obusek for assistance.

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Behavioral Measurement of Neural Poststimulation Excitability Cycle: Pain Cells in the Brain of the Rat

Abstract. *A new technique in which elicited behavior of the freely moving rat is used to measure the poststimulation excitability cycle of the central neurons mediating that behavior has been adapted from accepted methods of neurophysiology. A continuous train of pairs of brief pulses was delivered to pain systems in the midbrain. Rate of lever pressing to achieve 3-second rests from this stimulation was measured as a function of the interval separating the pulses within pairs. Evidence for latent addition, absolute refractory period, temporal summation, and adaptation was demonstrated. Obtained relationships suggested that three sets of fibers may carry the aversive signal and that synaptic integration of pain in the brain may be related to Stevens' power law functions.*

The differential responsiveness of an organism to the various temporal rates or patterns in which stimuli can occur is determined by the ability of the individual neurons and synapses in the pathways mediating the responses to accept and conduct stimuli at these rates and patterns. Thus, if one knew the excitability of the relevant neurons and synapses to various rates and patterns of stimulation, and if one could control or measure these rates and patterns, then the strength of the overt behavior might well be predicted. Furthermore, it is plausible to expect that the function expressing "response strength" in terms of "stimulus rate," which holds over a large range for overt behavior, should closely mimic in form the strength-rate function for the neurons subserving the behavior. This expectation is important to test because, if it proves in fact to be a general truth, one can then use the strength-rate function observed for any particular overt behavior to tell us much about the nature of the neurons and synapses mediating the connection between the stimulus input and the response output for that behavior.

In essence, this type of approach was employed early by Sherrington in his work on the neural organization of the spinal withdrawal reflex and has more recently been used, for example, by Barlow to study the phenomenon of temporal summation in the human retina (the Bunsen-Roscoe law). In these instances, rate or pattern of stimulation of receptors or peripheral nerves was varied, and a behavioral index such as a leg withdrawal or a verbal report was employed. However, to our knowledge no one has used electrodes to introduce the experimental manipulation of stimulus rate and pattern directly into the central nervous system in the context of this type of approach. We have done so with the idea that it may be possible thereby to analyze something of the nature of the neuronal and synaptic mechanisms underlying those complex behaviors which are organized in the brain.

The success of this approach depends upon first demonstrating that the strength-rate functions for electrically elicited overt behaviors are isomorphic with those obtaining for neurons. Fortunately, since the strength-rate functions for neurons have been generally identified, at least for the peripheral nervous system, it is possible to generate some predictions by which to test the validity of this approach. For example, the more rapidly a neuron is stimulated, the more likely it is that the postsynaptic neuron will fire because of the temporal summation of neurotransmitter in the synapse faster than it can be destroyed; thus, the strength of electrically elicited overt behavior should be greater as the interval between stimulus pulses is shortened. However, since neurons cannot fire to all the stimulus pulses if they follow each other too closely because neurons require a time to recover after each firing (the refractory period), the strength of the electrically elicited overt behavior should not continue to increase indefinitely as the interval between stimulus pulses is shortened, but should even decrease at those intervals falling within the refractory period. The details of our test of these and other predictions follow.

The techniques developed in our experiment were based upon those in which two 0.1-msec negative-going electrical pulses, one (the conditioning or C pulse) followed at a parametrically varied interval by another (the test or T pulse), were used as probes to explore the poststimulation excitability cycle of axons and synapses in the peripheral nervous system. Customarily the responses measured as a function of this interval separating the onsets of the C and T pulse (the C-T interval) were mainly action potentials, compound action potentials, and graded potential shifts recorded from short-term physiological preparations. The phenomena of latent addition, refractory period, super- and subnormality, temporal summation, and adaptation have been elucidated in this fashion, and an impressive correspondence between these phenomena and neuronal features such as size of axon diameter has been established. Our study was designed to show whether the same pattern of poststimulation excitability representative of the phenomena observed from peripheral nervous tissue can also be evidenced in the instru-

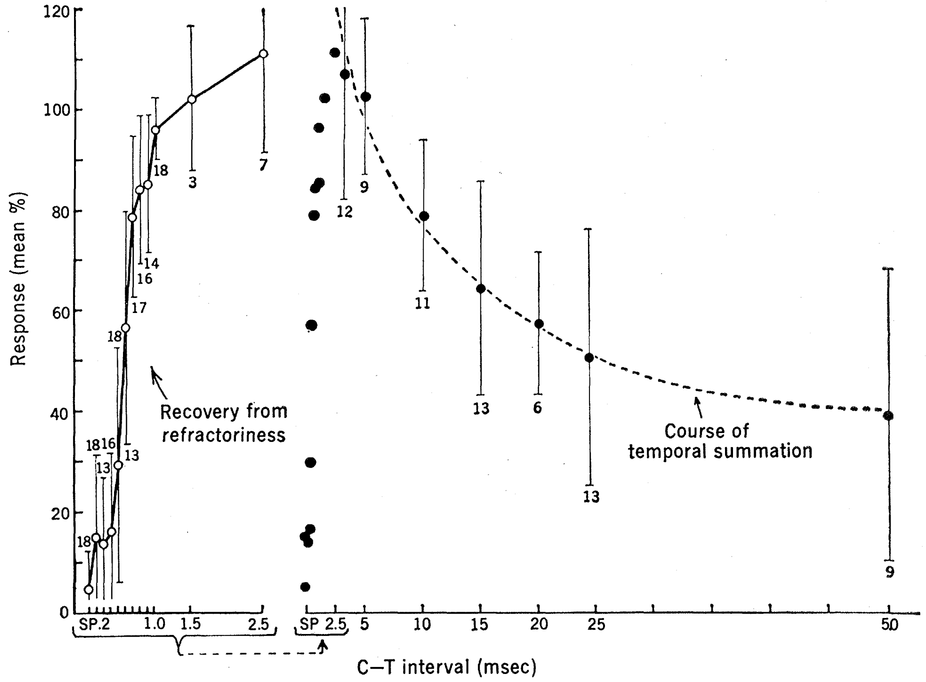

Fig. 1 Effect of size of C-T interval on rate of lever pressing to escape aversive brain stimulation. Before mean values for rates were computed they were transformed to percentages: the rate at each C-T interval minus the value of the lowest rate was divided by the difference between the rate at the 1.0-msec C-T interval and the lowest rate. The left-hand portion of the figure represents a replotting on a magnified abscissa of data points at the extremely short C-T intervals. The vertical lines represent the standard deviation of the percentage scores, and the numbers either above or below these vertical lines indicate the number of animals tested at each point.

mental escape responding of freely moving rats that have been electrically stimulated in central pain systems by a train of C and T pulses separated from each other by C-T intervals identical to those customarily employed. This use of trains of C and T pulse pairs constituted, however, a notable departure from the classical C-T technique in which only one C and one T pulse are used. This was necessary because administering a single pulse pair in the escape situation does not produce overt behavior. However, as later demonstrated, the same pattern of reponse as a function of C-T interval could be obtained for overt behavior with the use of trains, as recorded in cells when a single pulse pair was used.

To test the use of the C-T technique in behavior experiments (*1*), we studied the pain system because there already exists much information on neural structure and pain transmission against which to compare our findings and because we feel that our results may be useful in uncovering the complex neural code of pain. Although various theories (*2*) have attempted to account for the coding of pain signals in terms of the diameters of peripheral fibers or on the basis of synaptic properties of temporal and spatial summation, Melzack and Wall (*3*) have concluded that neither of these explanations is sufficient to account for the diverse phenomena to be explained. They propose that a synaptic gating mechanism in the spinal cord, controlled by both large and small fibers, mediates somesthetic pain stimuli to central cells which, if triggered, signal conscious pain. However, little is known of these central cells; they have been implicated in the transmission of pain signals mainly on the basis of their anatomical properties and have only been investigated with short-term physiological preparations (*4*). Accordingly, it is to this central level of the pain system that we have directed our behavioral study.

To establish the correlate between an organism's overt responding and the behavior of neurons, 18 male Sprague-Dawley rats were stimulated (*5*) in the midbrain by way of permanently implanted electrodes aimed either at the dorsolateral tegmentum, an area through which spinothalamic fibers are thought to pass (*6*), or at the medial lemniscus. Monopolar electrodes were used and were insulated to within 0.5 mm of the tip; an uninsulated jeweler's screw placed rostrally in the skull served as the ground. After the experiment, histological examination of electrode placement was correlated with the voltage required to elicit the aversive behavior. The sites where this voltage was lowest can be described with reference to the Konig and Klippel stereotaxic atlas of the rat brain (*7*) as follows: for the dorsolateral tegmentum electrodes these were (for plate 48b) A, 1.76; H, −0.6; L, 2.3; and (for plate 49b) A, 1.61; H, +0.5; L, 2.2. For the medial lemniscus electrodes (plate 50b), they were A, 1.27; H, −2.4; L, 1.4.

The stimulation consisted of a continuous train of paired C and T pulses delivered within a session both at a constant voltage and at a constant C-C interval (the interval separating the onset of each conditioning pulse from the onset of the preceding one). By pressing a lever an animal could interrupt this train for a 3-second rest and, thereby, escape the aversive stimulation for a brief time. The number of presses per 1-minute trial was recorded as a function of size of the C-T interval. Latency to make the first press was also often measured.

The details preliminary to testing were as follows: After recovery from implantation each rat was put in the test apparatus, a square box (30 cm on a side), and taught to press a lever in the box in order to turn off the stimulation. All animals showed a clearly aversive response to this stimulation, such as squealing, defecation, urination, and running. In addition, a pilot experiment was run on four of the rats to find out within what range of voltages the lever-pressing rate would increase as voltage was increased (*8*). This was necessary not only to validate that the lever-pressing measure could indeed be an adequate index of the motivational value of the brain stimulation levels to be used, but also to establish generally within what voltage limits this would remain true. Thus, a few pilot trials were always conducted before testing on each experimental session to select a constant voltage for use throughout that session. This was done in such a way that the C-T interval to which the animal responded with the greatest apparent discomfort produced a lever-pressing rate just short of the maximum rate at which the pressing measure remained sensitive.

Twenty to sixty trials, each separated by a 1-minute time out, constituted a daily session's test. The C-T interval was varied in a counterbalanced fashion from trial to trial. A single-pulse (SP) control condition in which the T pulses were omitted from the train was also tested during each session to provide a base line against which to evaluate the differential contribution of the T pulses at the various C-T intervals. The exact intervals employed and number of animals tested at each are indicated in Fig. 1. Although within a session the C-C interval was held constant, it was sometimes varied between sessions but always took one of the following values: 10, 25, 50, or 100 msec. The reason for using different C-C intervals was that, surprisingly, at the 10-msec interval many of the animals habituated within seconds to the aversive stimulation (*8*). Since stimulation at a high frequency may cause depression of neural response, the frequency was decreased by increasing the C-C interval. This manipulation of decreasing frequency stopped habituation; the animal now both pressed at a constant rate and appeared equally uncomfortable throughout the test period.

Figure 1 is a summary of results compiled elsewhere (*8*). To make a comparison of all animals, with respect to the shape of their C-T curves, in a way independent of differences in the absolute levels of their lever pressing, we converted each animal's scores to percentages (Fig. 1, legend). For the purpose of illustrating the main contour of the results, the data from the various C-C and electrode placement conditions were combined since they did not differ in this general respect.

Behavioral evidence for the axonal phenomena of latent addition and refractory period is given in the rising or left-hand portion of the curve in Fig. 1, and the evidence for the synaptic phenomena of temporal summation decay in the falling or right-hand portion. Behavioral latency data (not presented here) are in agreement with the findings.

Latent addition. A small peak followed by a trough occurred in escape responding at the 0.2-msec C-T interval. This was consonant with electrophysiological findings that a nerve fiber can store and summate charge capacitatively on its membrane for as long as a 0.2-msec interval, termed the period of latent addition (*9*). Thus, in the event that the C pulse does not fire all the fibers mediating aversive sensation, stimulation at such short C-T intervals should behaviorally produce a lever-pressing rate greater than that obtained under the SP or 0.3 msec C-T conditions, as indeed occurred.

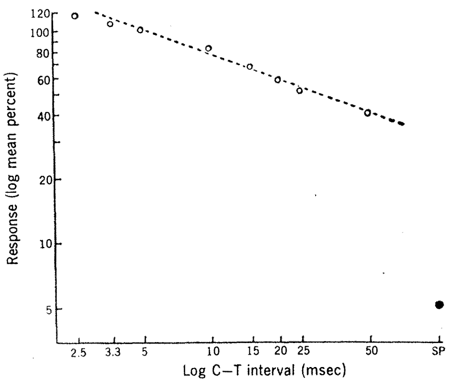

Fig. 2. Log-log transformation of the temporal summation portion of the curve shown in Fig. 1.

Absolute refractory period. From the C-T interval range between 0.4 to 0.9 msec there was first a highly significant sharp rise and then a leveling off in escape responding rate. From the 0.9- to 1.0-msec C-T intervals there was another sharp rise ($t = 3.12$; d.f. 13; $P < .01$). Finally, there was a gradual rise from 1.0- to 2.5-msec C-T intervals. We relate these findings to the absolute refractory period as follows: The absolute refractory period is a period of absolute inexcitability of a fiber immediately after its firing. The duration of this interval varies inversely as the diameter of the fiber stimulated and has been found to be 0.4 to 1.0 msec for A fibers, 1.2 msec for B fibers, and 2.0 msec for C fibers (*9–11*). Hence, behaviorally, when the C-T interval is very short and the T pulses arrive during the refractory period of the fibers, the response level should not differ from the control condition (SP) in which the T pulses are omitted from the train. However, as the C-T interval is increased, at some point the T pulses should begin arriving after the refractory period is over, and now should be effective in stimulating the fibers. At this point an increase in the escape response rate should occur, marking the end of the absolute refractory period. We should then be able to infer the refractory period from the duration of this period of lowered responding and, hence, also infer the size of the diameters of the fibers involved. Our initial response rise, from 0.4 to 0.9 msec, corresponds to the recovery time for the large diameter A alpha fibers. The second rise from 0.9 to 1.0 msec is consonant with the recovery from refractoriness of A delta fibers of somewhat smaller diameter. The third rise from 1.0 to 2.5 msec agrees with the recovery of small diameter C fibers from refractoriness. Since there was no assurance that the current levels were physiologically maximal, this rise may also reflect the recovery of some of the larger fibers from their relative refractory periods. There was some evidence that this final increment was mainly due to the dorsolateral tegmentum group.

Temporal summation decay. In the right-hand portion of Fig. 1 it is evident that, as the C-T interval was lengthened from 2.5 to 50.0 msec, a gradual drop in escape responding occurred. This is thought to reflect events taking place at the synapse rather than on the axon, since at these long intervals the C to T separation exceeds the refractory period, and the fibers will conduct both pulses to the synapse. We interpret this drop in escape responding to be due to temporal summation at the synapse (*12*, *13*) because the response decrement follows the shape observed in peripheral preparations (*11*, *14*), namely the larger the interval between pulses the smaller the response. One mechanism for such temporal summation is that, at small C-T intervals, neural transmitter is released into the synapse faster than it can be destroyed. Another mechanism is a presynaptic change wherein closely spaced pulses may each cause the release of more packets of transmitter from the presynaptic terminal (*13*, *15*).

The data for the temporal summation decay as represented on the untransformed scales of Fig. 1 is negatively decelerating, but when plotted on logarithmic scales (Fig. 2) the data describes a linearly decelerating power function with equation, $y = 200\,X^{-0.414}$ (*16*). This suggests that the Stevens' power law (*17*) relating physical intensity to "judged" intensity also holds in the present case of hypothesized synaptic intensity and behavioral intensity. If so, this demonstrates that such power transformations by the nervous system can occur centrally as well as at the receptors, since to obtain this function we have bypassed the peripheral receptors in stimulating pain (*18*). It should be noted that the decay time of the present effect greatly exceeds both the 14-msec decay time observed in spinal reflexes by Lloyd (*14*) and the 10-msec decay time in synaptic potentials of motoneurons found by Eccles (*19*). However, synaptic excitation of cortical pyramidal cells and thalamic neurons may give prolonged excitatory postsynaptic potentials of up to 80 msec (*20*) and inhibitory postsynaptic potentials in the brain often have durations exceeding 100 msec (*13*, *15*).

The remarkable isomorphism between the poststimulation neural excitability cycle and our behavioral results indicates that the same function expressing response strength in terms of stimulus rate holds for overt behavior as well as for neuronal behavior. This indicates that, with the C-T technique, the overt response of the organism can be a useful measure of the behavior of the neurons involved in mediating that response and also of their structural properties. In addition to the general importance in terms of the validity of the technique, the import of these results for the understanding of pain are as follows. (i) They suggest that several sizes of fibers are involved in mediating pain or aversion at the level of the midbrain. (ii) They indicate not only that the synaptic mechanism of temporal summation exists for pain at this midbrain level but also that it follows a surprisingly long time course and may be related to Stevens' power law. This relation is important since Stevens has thought that his law only applied at receptors (*21*). (iii) Taken together, points (i) and (ii) show that the type of coding of pain information as a function of fiber size and synaptic integration which Melzack and Wall (*3*) attribute to a gating mechanism in the spinal cord can also be produced at higher brain levels. (iv) The subsidiary finding that behavioral habituation to aversive brain stimulation occurs if fibers are stimulated too rapidly, as predictable from neural adaptation, suggests that this mechanism may be important centrally in the control of pain (*22*) and raises the possibility that some behavioral consequences of electrical stimulation are the result of central nervous tissue being shut off at certain frequencies of stimulation rather than excited. (v) Finally, since most of the phenomena used to explain the compound curve in this paper have been identified classically in preparations having none, one, or only a few synapses between input and output, the question arises as to why they are detectable in the complex multisynaptic preparation that is the conscious freely moving animal. One possible answer is that the precise timing of the C-T variable is lost at the first synapse and is thereafter reflected in different levels of general activity in higher pain mechanisms, of which the behavior is a linear function.

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References and Notes

1. One of us (J.A.D.) has applied the C-T technique to the behavioral measurement of refractory period and temporal summation in the self-stimulation system, respectively, as follows: J. A. Deutsch, *J. Comp. Physiol. Psychol.* **58**, 1 (1964); *Nature* **208**, 592 (1956).
2. W. H. Sweet, in *Handbook of Physiology, Section I; Neurophysiology* (American Physiological Society), J. Field, H. W. Magoun, V. E. Hall, Eds. (Wiliams & Wilkins, Baltimore, 1959), vol. 1, pp. 459–506; G. H. Bishop, *Brain* **26**, 77 (1946); D. C. Sinclair, *Brain* **78**, 584 (1955).
3. R. Melzack and P. D. Wall, in *Proceedings of the International Symposium on Pain*, J. Cahn and J. Charpentier, Eds. (Academic Press, New York, 1968), p. 11.
4. G. F. Poggio and V. B. Mountcastle, *J. Neurophysiol.* **26**, 755 (1963); M. Abeles, *Electroencephalogr. Clin. Neurophysiol.* **23**, 25 (1967).
5. A brain stimulator produced trains of capacitance-coupled negative-going pulse pairs which were administered to the animal through a 50K variable resistor that served as a voltage divider. All stimulation was constantly monitored on a Tektronix oscilloscope. The design of the brain stimulator has been described by J. A. Deutsch, *J. Exp. Anal. Behav.* **9**, 399 (1966).
6. K. E. Webster and R. D. Lund, *J. Anat.* **101**, 847 (1967).
7. J. F. R. Konig and R. A. Klippel, *The Rat Brain: A Stereotaxic Atlas of the Forebrain and Lower Parts of the Brain Stem* (Williams & Wilkins, Baltimore, 1963).
8. For detailed information see R. S. Kestenbaum, thesis, New York University (1968).
9. K. Lucas, *J. Physiol.* **39**, 461 (1910).
10. J. Erlanger and H. S. Gasser, *Electrical Signs of Nervous Activity* (Humphrey Milford: Oxford University Press, London, 1937).
11. J. B. Hursh, *Amer. J. Physiol.* **127**, 140 (1939); H. S. Gasser and H. Grundfest, *J. Physiol.* **117**, 113 (1936); H. Grundfest, *Ann. Rev. Physiol.* **2**, 213 (1940).
12. As an alternate to temporal summation, it is also possible that the drop in escape responding at progressively larger C-T intervals may be due to a related phenomenon termed temporal facilitation. Bullock and Horridge, in a glossary of terms, distinguish between temporal facilitation and temporal summation as follows (*13*, p. 1600). "The former is shown by an additional effect of a second stimulus over and above the summed effects of the first and second stimuli if these had been separate. Thus simple linear summation of contractions or potentials is excluded from facilitation."
13. T. H. Bullock and G. A. Horridge, *Structure and Function in the Nervous System of Invertebrates* (Freeman, San Francisco, 1965).
14. D. P. C. Lloyd, *J. Neurophysiol.* **9**, 421 (1946).
15. J. C. Eccles, *The Physiology of Synapses* (Springer-Verlag, Berlin, 1964).
16. We thank R. A. Young, a graduate student at New York University, for pointing out to us the log-log linearity of our temporal summation results.

→ S. S. Stevens, *Psychol. Rev.* **64**, 153 (1957).

18. Because of the proximity of the dorsolateral tegmentum placement to the medial geniculate we cannot rule out the possibility of aversive acoustical sensation being produced by stimulation at that placement. However, since the medial lemniscus placement also produced the same results, they cannot be attributed only to acoustical effects.
19. J. C. Eccles, *J. Neurophysiol.* **9**, 87 (1946).
20. C. G. Phillips, in *The Nature of Sleep*, G. E. W. Wolstenholme and M. O'Connor, Eds. (Churchill, London, 1961), p. 26; C. Li and S. N. Chou, *J. Cell. Comp. Physiol.* **60**, 1 (1962).
21. S. S. Stevens, in *Sensory Communication*, W. A. Rosenblith, Ed. (M.I.T. Press, Cambridge, Mass., 1969).
22. P. D. Wall and W. H. Sweet, *Science* **155**, 108 (1967); D. V. Reynolds, *Science* **164**, 44 (1969).
23. Suppored by NIMH predoctoral fellowship 4-F1-MH31011 to R.S.K.; NSF grant GB-5400 and NIMH grant MH-12766-01 to J.A.D.; NIH biomedical science support grant to New York University (E.E.C.).

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Earthquake Occurrence in the State of Washington

Year before last, my student C. H. Cramer, then an undergraduate at the University of Puget Sound, Tacoma, Washington, prepared a time-lapse moving picture of earthquake occurrences in the State of Washington that is an interesting counterpart of Richter's analysis (*1*). The background is the state geologic map; two frames correspond to 1 day, and earthquakes are shown as light flashes, the location being that of the epicenter and the brightness of the flash being a measure of the magnitude of the earthquake.

When the film is viewed (for this purpose a manual editor-viewer, with which the film can be moved forward or backward at an arbitrary speed, is superior to a regular projector), it reveals a remarkable story of alignments of epicenters, earthquake swarms, stress buildup and release, and other features. The lines along which earthquake swarms occur are in complete agreement with offsets of gravity trends revealed by my analysis (*2*). Moreover, those lines, cutting across the Cascade Mountains, pass almost exactly through the andesitic Cascade volcanoes.

Is it, then, conceivable that the volcanoes develop along those planes of offset where fresh basalts come in contact with the acidic batholith, and are thus quartz-enriched?

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References

1. C. F. Richter, *Science* **166**, 173 (1969).
2. Z. F. Daneš, *Eos* **50**, 548 (1969); "Gravity and Tectonism in Washington," in preparation.

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