

## Self-Stimulation Alters Human Sensory Brain Responses

**Abstract.** Human electrocortical potentials evoked by self-administered auditory and visual stimuli manifest much smaller amplitude and faster poststimulus timing than do average brain responses evoked by identical machine-delivered stimuli. Auditory evoked potentials show this "self-stimulation effect" to a greater degree than do visual responses. For visual evoked potentials, the effect appears greater at the vertex association area than over the occipital cortex. Individual differences in the magnitude of the "self-stimulation effect" relate to level of intelligence.

The brain's control of its sensory input poses a significant problem for neurophysiology. The average evoked potential from the intact scalp provides a reliable measure of the human brain's electrocortical encoding of visual, auditory, and tactile sensory input (1). The amplitude of auditory evoked potentials varies with the rate of stimulation (2, 3), a result suggesting that some neural process exists which modulates the brain's response to sensory input.

Self-stimulation, in contrast to machine-controlled stimulus delivery, allows one to study possible differences in sensory evoked potentials to physically identical stimuli about whose timing the brain possesses varying degrees of foreknowledge. If such evoked potential differences do exist, they could indicate a relation between cognitive functions and the neural activity underlying sensory information processing.

We now report results from 50 humans, ranging in age from 3 to 78 years and in intelligence level from institutionalized retardates to Ph.D. scientists, which demonstrate that average electrocortical potentials evoked by self-delivered auditory and visual stimuli exhibit much smaller amplitude and significantly faster poststimulus timing than do brain responses evoked by identical stimuli about whose timing the person has no foreknowledge, a cognitive function. Individual differences in the magnitude of this "self-stimulation effect" appear related to level of intelligence.

The average auditory evoked response from the vertex (Cz-A1 in the 10-20 system) and the average visual evoked response from occipital (Oz-A2) and vertex derivations under three conditions of stimulation (periodic, machine-delivered, and self-stimulation) served as the basic data. Auditory stimuli consisted of clicks of 1-msec duration delivered at 80-db sound level by a loudspeaker placed 0.6 m above the subject. For visual stimulation, subjects sat in a darkened, shielded enclosure watching a frosted window transillumi-

nated by bright photic stimuli of 10- $\mu$ sec duration. Each experiment comprised four stimulation conditions whose order we counterbalanced across experiments: self-stimulation, in which the subject delivered flash or click stimuli to himself by pressing a hand-held microswitch, with some attempt to deliver the stimuli randomly in time; machine stimulation, consisting of tape recorder playback of the stimulus sequence generated by the subject during the self-stimulation condition; periodic stimulation, with clicks or flashes presented regularly at the rate of one every 2 seconds (4); and self-stimulation control, in which the subject pressed the microswitch but received no stimulus accompanying this action. Through use of a pulse generator connected directly to the loudspeaker and the photic stimulator and triggered by the subject's

finger press, by tape-recorded marker pulses, or by an oscillator set to fire every 2 seconds, we held all stimulus variables except timing constant across these conditions, and even stimulus timing remained constant between the self- and machine-stimulation conditions.

We obtained an evoked cortical response for each of these conditions from nine young adults (five male, four female) by using a PDP-8 computer that averaged 100 responses over a 500-msec poststimulus interval using a 500-hertz digitization rate. The computer scored these evoked responses for the poststimulus latency of all reliable components detected and for integrated amplitude (the total area under the curve of the evoked response wave form). Using the *t*-test for correlated pairs of means, we then statistically analyzed these latency and amplitude values to determine possible differences related to the three conditions of stimulation. We also examined the averaged brain activity taken under the self-stimulation control condition for the presence of potentially confounding pre- and postmovement vertex potentials time-locked to the subject's finger movement. Only two subjects in our initial experiments produced such

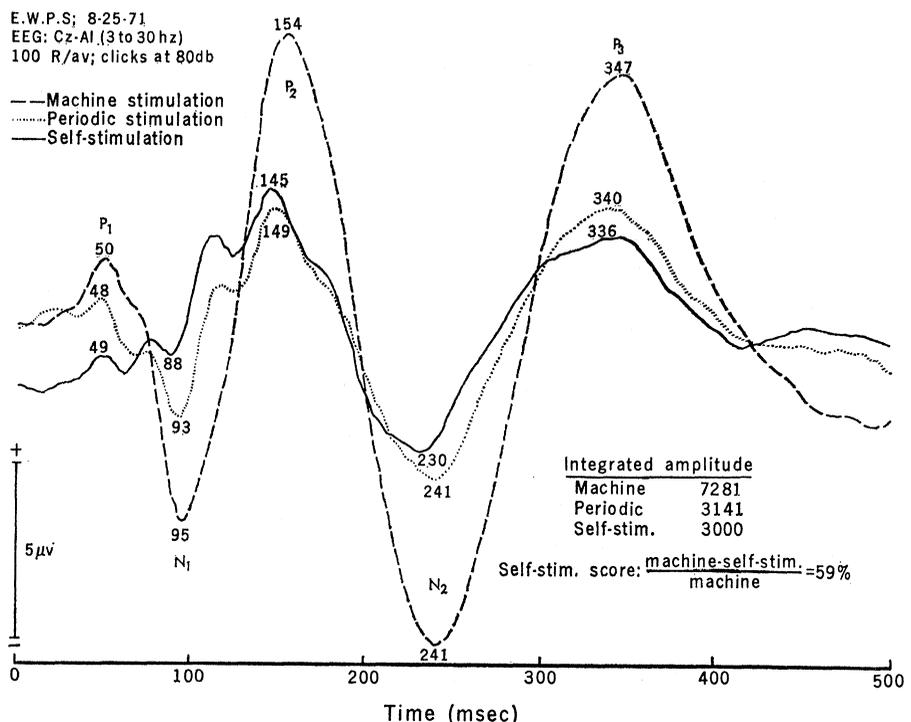


Fig. 1. Wave forms of average auditory evoked responses for E.W.P.S. under three conditions of stimulation. Numbers beside each component ( $P_1$  to  $P_3$ ) correspond to poststimulus latency values in milliseconds. Note characteristically smaller amplitude and faster component latencies for self-evoked in contrast to machine-evoked responses. Amplitude and latency values for potentials evoked by periodic stimulation fall between those for the self- and machine-evoked responses; EEG, electroencephalogram; R/av, responses per average.

Table 1. Mean percentage of differences and associated statistical significance levels between evoked responses from nine subjects under three stimulation conditions. Note significantly smaller amplitude and faster latency for self-delivered as opposed to machine-delivered stimuli, with responses to periodically presented auditory stimuli falling between and differing significantly from these values; NS, not significant.

Modality	Area	Variable	Machine—self		Machine—periodic		Periodic—self	
			Per-cent	P	Per-cent	P	Per-cent	P
Auditory	Vertex	Latency	5	.001	3	.02	2	.02
Auditory	Vertex	Amplitude	50	.005	34	.01	16	.05
Visual	Vertex	Latency	4	.02	2	.05	2	NS
Visual	Vertex	Amplitude	28	.01	15	NS	13	NS
Visual	Occiput	Latency	5	.005	1	NS	4	NS
Visual	Occiput	Amplitude	-3	NS	-4	NS	2	NS

“command” or “motor” potentials (5), but these potentials disappeared when the same subjects triggered the stimulus with the index finger instead of thumb. In all subsequent experiments, to eliminate any possible contamination of the self-evoked response, subjects used the index finger of the dominant hand to initiate stimulus delivery.

Initial results (Table 1 and Fig. 1) demonstrate that electrocortical potentials evoked by self-delivered visual and auditory stimuli exhibited much smaller amplitude and faster post-stimulus timing than did responses evoked by identical machine-delivered stimuli. Auditory evoked potentials showed this “self-stimulation effect” to a greater degree than did visual evoked responses. We observed no self-stimulation effect on amplitude for visual responses from the occipital pole, whereas simultaneously recorded potentials from the vertex showed a significant 28 percent difference between the machine- and self-stimulation conditions. The amplitude and latency of the auditory responses evoked by periodic stimulation occupied a middle ground between and differed significantly from the self- and machine-evoked responses. For vertex potentials evoked by both auditory and visual stimuli, the amplitude differences (50 and 28 percent) between machine- and self-evoked responses greatly exceeded the latency differences (5 and 4 percent). Individual component analysis of vertex responses to auditory stimuli revealed no significant self-stimulation effects for the early  $P_1$  component, while later components beginning with  $N_1$  and continuing through  $P_3$  showed significantly smaller amplitude and faster latency for responses to self-administered stimuli. These results favor a concept of functional specificity for vertex evoked potential components

(3, 6). While early, sensory-specific components do not show the self-stimulation effect, later, nonspecific components thought to reflect cognitive functions manifest the effect to a significant degree.

One can argue that in our experimental paradigm, subjects possessed complete foreknowledge of stimulus timing when they stimulated themselves, no foreknowledge when the machine delivered the stimuli randomly in time, and some foreknowledge based on memory of the preceding stimulus sequence when stimuli occurred regularly every 2 seconds. Results indicate, therefore, that the more foreknowledge the brain has of stimulus timing, the smaller and faster the electrocortical potentials evoked by that stimulus. Foreknowledge of stimulus modality

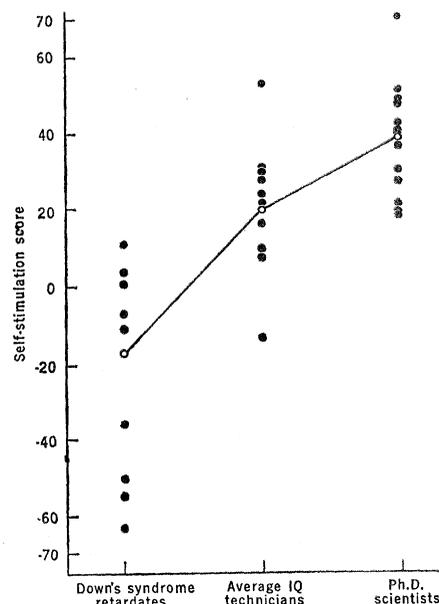


Fig. 2. Self-stimulation scores for 9 retardates with Down's syndrome, 10 technicians of average intelligence, and 13 Ph.D. scientists. Points connected represent the mean scores for the three groups.

(7), stimulus pitch (8), stimulus delivery (9), stimulus location (10), and stimulus intensity (11) modulate the amplitude of vertex association potentials in a similar manner. These and other results (12) point to a basic relation between cognitive functions and the neural activity underlying sensory information processing.

Directed by these initial findings, our subsequent research on the self-stimulation effect has concentrated on the amplitude of vertex evoked potentials to auditory stimuli. We devised a “self-stimulation score”—speculatively, the brain voltage “saved” when responding to self-delivered as opposed to machine-delivered click stimuli; technically, the percentage of difference between the total integrated voltage of vertex potentials evoked by 50 self-delivered and 50 machine-delivered click stimuli at a sound level of 80 db (Fig. 1). This score showed wide inter-individual variation (13) and impressive test-retest reliability (Spearman  $\rho$  of .92; 13 subjects) with no statistical difference between first and second measures taken from 30 minutes to 6 months apart (modal test-retest interval of 6 days). Twenty-eight measures on one of us (E.W.P.S.) made over a 19-month period generated a mean self-stimulation score of 54 percent with a standard error of only 3 percent, results indicating sound long-term stability. These scores ranged, however, from 21 to 76 percent, with low scores seeming to coincide with periods of fatigue or illness. These subjective observations suggested a possible relation between level of cognitive efficiency and the self-stimulation score. Consistent with this hypothesis, results from seven subjects have demonstrated that moderate consumption of ethanol results in a significant, dose-related decrease in the self-stimulation score (14). The amplitude of the machine-evoked response decreased markedly 40 minutes after a moderate dosage of ethanol (1 ml of 98 percent ethanol per kilogram of body weight) as reported (15), while the amplitude of the self-evoked response remained essentially unchanged. Heavy dosage (2 ml/kg), however, not only reduced the machine-evoked response further, but also produced a definite amplitude decrease in the self-evoked response.

Prompted by substantial individual differences in the self-stimulation score and evidence relating aspects of the sensory evoked response to human intelligence (16), we then looked for a

possible relation between level of cognitive ability and the self-stimulation score. Results from 9 retardates with Down's syndrome, 10 technicians selected for average intelligence (Peabody IQ between 90 and 110), and 13 Ph.D. scientists indicate a definite positive relation between intelligence level and the self-stimulation score (Fig. 2). The scientists scored higher than the technicians, who in turn outscored the retardates (17). For a majority of the Down's syndrome patients, the amplitude of the self-evoked response actually exceeded that of the machine-evoked potential. In contrast, all but one of the subjects with normal intelligence showed the expected self-stimulation effect. These results could enhance the usefulness of the sensory evoked potential for understanding and perhaps measuring the biological substrate of individual differences in behavioral intelligence.

Finally, because initial results had implicated foreknowledge or short-term memory as a correlate of the self-stimulation effect, we conducted seven experiments on E.W.P.S. exploring the possible effects of delaying delivery of self-administered stimuli by a fixed time. We found that the self-stimulation score decreased linearly with progressively longer delays of the stimulus, but that even with delays of up to 4 seconds some residual self-stimulation effect remained, in that the amplitude of self-evoked responses still fell below that of machine-evoked responses. These results indicate that the brain studied could functionally "remember" for up to 4 seconds that it had stimulated itself. The paradigm of self-stimulation with delay should prove useful for studying short-term memory function at the fundamental electrocortical level (18).

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#### References and Notes

1. H. E. Whipple, Ed., *Ann. N.Y. Acad. Sci.* **112** (1964), entire volume; E. Donchin and D. B. Lindsley, Eds., *Average Evoked Potentials: Methods, Results and Evaluations* (Sp-191, National Aeronautics and Space Administration, Washington, D.C., 1969); D. Regan, *Evoked Potentials in Psychology, Sensory Physiology and Clinical Medicine* (Chapman & Hall, London, 1972); C. Shagass, *Evoked Brain Potentials in Psychiatry* (Plenum, New York, 1972).
2. H. Davis, T. Mast, N. Yoshie, S. Zerlin, *Electroencephalogr. Clin. Neurophysiol.* **21**, 105 (1966); D. A. Nelson and F. M. Lassman, *J. Acoust. Soc. Amer.* **44**, 1529 (1968); R. A. Butler, M. Spreng, W. D. Keidel, *Psychophysiology* **5**, 665 (1969); H. H. Rothman,

- H. Davis, I. S. Hay, *Electroencephalogr. Clin. Neurophysiol.* **29**, 225 (1970).
3. A. Ohman, J. J. Kaye, M. Lader, *Psychonom. Sci.* **27**, 275 (1972).
4. We selected the 2-second interstimulus interval for the periodic condition because pilot studies had shown that the average interstimulus interval for the self-stimulation condition corresponded to approximately this value.
5. L. Gilden, H. G. Vaughan, Jr., L. D. Costa, *Electroencephalogr. Clin. Neurophysiol.* **20**, 433 (1966); E. W. P. Schafer, *Nature* **216**, 1338 (1967); H. G. Vaughan, Jr., L. D. Costa, W. Ritter, *Electroencephalogr. Clin. Neurophysiol.* **25**, 1 (1968); L. Deke, P. Scheid, H. H. Kornhuber, *Exp. Brain Res.* **7**, 158 (1969).
6. R. T. Wilkinson and H. C. Morlock, *Electroencephalogr. Clin. Neurophysiol.* **23**, 50 (1967); W. R. Goff, in *Attention in Neurophysiology*, C. R. Evans and T. B. Mulholland, Eds. (Butterworth, London, 1969), pp. 169-193; H. Bostock and M. J. Jarvis, *Electroencephalogr. Clin. Neurophysiol.* **29**, 137 (1970); H. G. Vaughan, Jr., and W. Ritter, *ibid.* **28**, 360 (1970); D. A. Benson and D. C. Teas, *Percept. Psychophys.* **11**, 203 (1972); A. Ohman and M. Lader, *Physiol. Behav.* **8**, 79 (1972).
7. S. Sutton, M. Braren, J. Zubin, *Science* **150**, 1187 (1965).
8. W. Ritter, H. G. Vaughan, Jr., L. D. Costa, *Electroencephalogr. Clin. Neurophysiol.* **25**, 550 (1968); P. Tueting, S. Sutton, J. Zubin, *Psychophysiology* **7**, 385 (1971); W. T. Roth, *ibid.* **10**, 125 (1973).
9. S. Sutton, P. Tueting, J. Zubin, E. R. John, *Science* **155**, 1436 (1967).
10. R. A. Butler, *Neuropsychologia* **10**, 219 (1972).
11. H. Begleiter, B. Porjesz, C. Yerre, B. Kissin, *Science* **179**, 814 (1973).
12. W. Ritter and H. G. Vaughan, Jr., *ibid.* **164**, 326 (1969); G. C. Sheatz and R. M. Chapman, *Electroencephalogr. Clin. Neurophysiol.* **26**, 468 (1969); J. Debecker and J. E. Desmedt, *Nature New Biol.* **234**, 118 (1971); L. E. Wilson, M. R. Harter, H. H. Wells, *Electroencephalogr. Clin. Neurophysiol.* **34**, 15 (1973).
13. Of the 41 nonretarded subjects tested to date, only 4 failed to give the characteristic amplitude variations between machine- and self-evoked responses shown in Fig. 1. These subjects, all female, gave self-evoked auditory vertex potentials with a qualitatively unique wave form characterized by a prominent positive component at 250 msec.
14. The 48 percent mean score with no drug differed significantly from the 20 percent mean score with ethanol ( $t = 5.62$ ;  $d.f. = 6$ ;  $P < .001$ ).
15. M. M. Gross, H. Begleiter, M. Tobin, B. Kissin, *J. Nerv. Ment. Dis.* **143**, 153 (1966); H. Fruhstorfer and P. Soveri, *Acta Physiol. Scand.* **74**, 26A (1968); E. G. Lewis, R. E. Dustman, E. C. Beck, *Electroencephalogr. Clin. Neurophysiol.* **28**, 202 (1970).
16. A. B. Barnett and A. Lodge, *Nature* **214**, 252 (1967); J. P. Ertl and E. W. P. Schafer, *ibid.* **223**, 421 (1969); L. E. Rhodes, R. E. Dustman, E. C. Beck, *Electroencephalogr. Clin. Neurophysiol.* **27**, 364 (1969); B. V. Butler and R. Engel, *Develop. Med. Child Neurol.* **11**, 77 (1969); M. M. Marcus, *Clin. Res.* **18**, 206 (1970); H. B. Bigum, R. E. Dustman, E. C. Beck, *Electroencephalogr. Clin. Neurophysiol.* **28**, 576 (1970); G. C. Galbraith, J. B. Gliddon, J. Busk, *Amer. J. Ment. Defic.* **75**, 341 (1970); D. W. Shucard and J. L. Horn, *J. Comp. Physiol. Psychol.* **78**, 59 (1972).
17. The scientist's mean self-stimulation score of 39 percent significantly exceeded the 21 percent mean score of the technicians ( $t = 2.61$ ;  $d.f. = 21$ ;  $P < .02$ ), who in turn scored significantly higher than the -17 percent mean score of the retardates ( $t = 3.24$ ;  $d.f. = 17$ ;  $P < .005$ ).
18. It came to our attention after completion of this study that our findings of a self-stimulation effect in human electrocortical responses relate to and show consistency with earlier work with monkeys [S. S. Fox, *J. Comp. Physiol. Psychol.* **58**, 225 (1964)].
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## Induction of Mating Behavior in Rats by Luteinizing Hormone-Releasing Factor

**Abstract.** *Ovariectomized female rats treated with estrogen, in dosages too low to provoke mating, displayed this behavior when given subcutaneous injections of synthetic luteinizing hormone-releasing factor (LRF) 48 hours later. Two hours after the injection of LRF, components of female sexual behavior appeared. The lordosis reflex followed mounting by the male, and darting and hopping behavior was quite prevalent. On the other hand, treatment with estrogen followed by luteinizing hormone, follicle-stimulating hormone, or thyrotropin-releasing factor did not induce copulatory behavior. The results suggest that LRF may play a role in induction of mating behavior.*

It has been clearly demonstrated that sexual behavior in subprimate female mammals is dependent on the ovarian steroids, estrogen and progesterone (1). In the female rodent, there is a clear relationship between the ovarian cycle on the one hand and rhythms of sexual receptivity on the other (2). Removal of the ovaries results in the complete cessation of estrous behavior. The heat response can be reinitiated by exogenous treatment with daily doses of estrogen over a period of days (3) or with relatively small doses of estrogen followed by progesterone (4). The ovarian cycle is

regulated by the gonadotropins from the anterior pituitary: follicle-stimulating hormone (FSH) to stimulate follicular development and luteinizing hormone (LH) to produce ovulation and formation of the corpora lutea (5). The output of ovarian steroids is similarly under the control of the gonadotropins (6) which, in turn, are under hypothalamic regulation mediated by hypothalamic-releasing factors (7). These factors are released into the capillaries of the hypophyseal portal system of veins and are carried down the pituitary stalk to reach the pituitary sinusoids where they trigger release of