and their afferent impulses can be recorded in the superior colliculus as well as in other brain loci involved with eye movements[11]. Cooper et al.[11] also found evidence of limb proprioceptor afferent connections in the same brain areas. Although Pickering and Varju[6] stated that optic nerve efferents do not contribute to the delayed-off responses, the present study suggests the possibility that the processing of after-images is modifiable centrally. Furthermore, the Popovs[12] have demonstrated that after-images can be obtained by conditioned reflex responses to sound!

Graham and Pong[7] hypothesize feedback loops within the amacrine-bipolar dyads of the retina which regulate ganglion cell output and are mediated through GABA-minergic systems. The time-course of GABA depolarization in primary afferent muscle spindle neurons[13], bears temporal resemblance to the positive after-image time-course resulting from ultra-short light stimuli. GABA, however, is only 1 of a number of putative inhibitory neurotransmitters present in the visual and central nervous system[14]. The present study of positive after-images and their erasure by saccadic movement suggests that there is an apparently time-linked latching mechanism that is unmasked by very brief light stimuli. The latching mechanism possibly causes storage of the transmitted retinal image in the visual cortex or at an intermediate locus. Under steady state illumination it maintains a stationary image while the micro-saccadic activity of the eye involves other receptors to fix the same point in space. The concomitant latching and unlatching through the intervention of excitatory and inhibitory neurotransmitters is perhaps the 'neuronic shutter mechanism' proposed by Lindsley[15] to explain why one perceives images while scanning that are stable and stationary, with clarity.

A 2-sec PAI resulting from a 10-μsec stimulus represents an amplification factor of 2×10^5. This finding has far-reaching implications with respect to subliminal perception, education and even thought control.

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GABAergic inhibition of neurons in the ventral tegmental area

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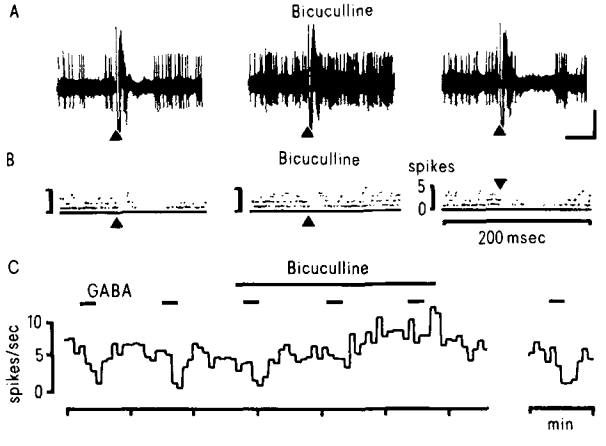
Summary. Stimulation of the nucleus accumbens evokes a potent inhibition in neurons of the ventral tegmental area. GABA is likely to act as a transmitter in this descending inhibitory system.

Neurons originating in the ventral tegmental area (VTA) have diffuse projections to subcortical limbic structures[1,2]. This mesolimbic system has recently received considerable attention because of its possible involvement in the pathogenesis of schizophrenia[1,3]. Biochemical[3] and behavioral[4] experiments have provided indirect evidence to suggest that there is a preferential inhibitory modulation of VTA neurons by GABAergic pathways descending from the limbic forebrain. This possibility was examined more directly in the present study by using microelectrode recording and microiontophoretic techniques.

Materials and methods. 10 male rats (200–400 g) were anesthetized with urethane (1.3 g/kg i.p.) and mounted in a stereotaxic frame. Multibarrel glass micropipettes (2–4 barrels, 3–5 μm tip diameter) were used for recording and microiontophoretic application of the following substances: gamma-aminobutyric acid (GABA, 0.5 M, pH 3.5), bicuculline methiodide (20 mM in 165 mM NaCl, pH 3.5) and pontamine sky blue (2% in 0.5 M acetic acid). The micropipettes were placed stereotaxically in the VTA using the atlas of De Groot[5] and the location of the micropipettes was marked by ejecting pontamine sky blue from the tips. The nucleus accumbens septi was stimulated by small bipolar electrodes which were also used to make electrolytic lesions at the termination of the experiments to verify the stimulation sites.

Results and discussion. Stimulation of the nucleus accumbens (1–20 V, 0.2–0.5 msec) evoked patterns of inhibition and excitation in neurons of the VTA similar to those



A Inhibition of a VTA neuron by stimulation of the nucleus accumbens (left trace), antagonized by iontophoretically applied bicuculline methiodide (100 nA, 3 min, middle trace) and recovery of the inhibition 6 min after withdrawal of bicuculline. 6 superimposed sweeps. Triangles mark the time of stimulation of the nucleus accumbens (10 V, 0.5 msec). Calibration: 40 msec; 1 mV.
B Same neuron as in *A*: peristimulus-time-histograms. 64 sweeps, 205 bins, 200 msec duration.
C Reversible block of depressant actions of GABA (40 nA) by microiontophoretically applied bicuculline methiodide (50 nA). Gap represents 6 min.

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described for nigral neurons after striatal stimulation[6–11]. Complex patterns consisting of brief excitation preceding the inhibition, an excitation interrupting a long period of inhibition or reverberating patterns were seen more often than short latency simple inhibitions. Out of 46 cells inhibited by accumbens stimulation, 15 demonstrated an inhibition with a latency of less than 10 msec and a duration of up to 250 msec.

Microiontophoretically applied GABA also readily inhibited VTA neurons with ejection currents usually below 20 nA. Application of bicuculline methiodide, a GABA antagonist[9,10,12] (20–100 nA, 3–10 min), often produced a slow increase in firing rate and reversibly antagonized the inhibition evoked by accumbens stimulation (10 of 13 cells) or local administration of GABA (3 cells). Examples are illustrated in the figure. None of these cells could be invaded antidromically by stimulation of the nucleus accumbens, an observation which is in line with the findings of Dray et al.[10] in the substantia nigra.

These results suggest that VTA neurons are inhibited by pathways descending from the nucleus accumbens and that this inhibition is GABA mediated. One might assume that this potent inhibition, even if mediated through interneurons, impedes the antidromic invasion of VTA cells from the nucleus accumbens. A GABAergic inhibition of neurons in the substantia nigra by fibres descending from the striatum has previously been demonstrated in the rat[9,10] and cat[8,13]. From our results it is likely that a similar inhibitory system exists between the limbic forebrain and the ventral tegmental area.

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Serotoninstoffwechsel bei chronischem Alkoholismus

Serotonin metabolism in chronic alcoholism

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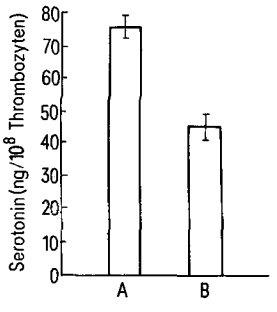
Summary. Serotonin was determined in platelets of 47 patients with alcoholism during the state of withdrawal as well as in a group of healthy persons. The results show that serotonin values were significantly lower in the group of patients with alcoholism as compared with the control group of healthy persons.

Beim Menschen wie auch tierexperimentell wurden Veränderungen im Serotoninstoffwechsel unter Einwirkung von Äthanol beschrieben. Olsen et al.[1] fanden bei Patienten mit chronischem Alkoholismus die 24-h-Harnausscheidung von 5-Hydroxyindolessigsäure im Vergleich zu einer Kontrollgruppe signifikant erniedrigt. Entsprechende Befunde wurden nach Verabreichung von Äthanol an Normalpersonen erhoben[2]. Diese Ergebnisse zusammen mit einer gleichzeitigen Erhöhung von 5-Hydroxytryptophol wurden im Sinne einer kompetitiven Hemmung des oxydativen Serotoninabbaus zugunsten des reduktiven Weges zu 5-Hydroxytryptophol interpretiert[3]; hierbei wurde diese Hemmung dem beim Äthanolabbau entstehenden Acetaldehyd zugeordnet[4]. Tierexperimentell zeigten sich zum Teil unterschiedliche Ergebnisse. Im Hirnstamm des Kaninchens fanden sich deutliche Verminderungen von Serotonin und Noradrenalin nach i.v. Gaben von Äthanol[5], ein Befund, der auf eine entspeichernde Wirkung des Acetaldehyds zurückgeführt wurde[6]. Im Mäusegehirn zeigte sich nach Äthanolgaben bei gleichbleibenden Serotoninwerten eine Erhöhung von 5-Hydroxyindolessigsäure; dieser Befund wurde als Folge eines Transportdefektes für 5-Hydroxyindolessigsäure gedeutet[7]. Aufgrund von Untersuchungen an Rattengehirnhomogenaten wurde weiterhin die Möglichkeit der Bildung einer intermediären Schiffschen Base aus Acetyldehyd und Noradrenalin bzw. Serotonin mit nachfolgender spontaner molekularer Reorganisation und Entstehung von Isochinolinalkaloiden postuliert. Dieser Vorgang wurde als möglicher suchterzeugender Faktor des



Serotonin in Thrombozyten bei gesunden Personen im Vergleich zu Patienten mit Alkoholismus im Stadium des Entzuges. *A*, Gesunde Personen (n = 11); *B*, Patienten mit Alkoholismus (n = 47). Die Säulen repräsentieren Mittelwerte, ± SEM.

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