the mesolimbic/mesocortical DA pathway (Thierry, Blanc, Sobel, Stinus & Glowinski, 1973; Ungerstedt, 1971). We have recently reported that infusions of SP (3 μg/1 μl) into the VTA of awake rats induce a behavioural activation characterized by increased locomotion and exploration (Iversen, Joyce, Kelley & Stinus, 1978). This activation is attenuated by 6-OHDA lesions of the terminals of the ascending DA-A10 pathway and also by local infusion of haloperidol into terminal regions of this pathway; thus it has been postulated that application of SP into the VTA activates the DA-A10 system (Stinus, Kelley & Iversen, 1978).

In order to investigate further this behavioural response, the effect of varying doses of SP infusion into the VTA was measured. Eleven male Sprague-Dawley rats were implanted with bilateral stainless steel cannula guides aimed at the VTA. Behavioural testing began one week after surgery. Activity was recorded in individual cages equipped with two photocells; the rats were well habituated to the cages before drug infusion began. During a test session the rats received bilateral infusion into the VTA of either saline (0.9%), 50 ng, 500 ng, or 3 μg of SP (Bachem); infusions were given in a latin square design. After infusion the rat was returned to the photocell cage and activity recordings were taken every 10 min for 1 hour.

SP elicited a dose dependent increase in locomotor activity (total photocell counts/h ± s.e.: saline 269 ± 57, 50 ng 413 ± 79, 500 ng 515 ± 152, 3 μg 843 ± 225). The response to the highest dose of SP was pronounced and levels of activity remained elevated throughout the hour test session. Interestingly, 50 and 500 ng SP induced an activation comparable to 3 μg during the first 10 min; however duration of SP effects after the lower doses was considerably reduced.

This experiment has demonstrated that the locomotor response to SP infusion into the VTA is dose dependent, and that a behavioural stimulation can be elicited with much lower doses than we have previously used. Further work is needed to elucidate the specificity and physiological basis of this response, and to understand the functional role of endogenous SP.

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The effects of 5,7-dihydroxytryptamine lesions of the median and of the dorsal raphe nuclei on social interaction in the rat

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Lesions of the median (MRN) and dorsal (DRN) raphe nuclei were produced by microinjections of 5,7-dihydroxytryptamine (4 μg in 1 μl injected over 5 minutes). Controls received equal volume injections of vehicle.

Rats in each lesion group were assigned to 3 of the social interaction test conditions: low light, familiar; low light, unfamiliar; high light, unfamiliar. Those allocated to the 'familiar' condition were placed singly in the test arena for two 10 min periods prior to the social interaction test. Those in the 'unfamiliar' conditions were placed in the test room under the appropriate light level, but remained in their home cages. During the social interaction test pairs of male rats were observed for 10 mins and the time spent in active social interaction was scored. For details see File & Hyde (1978).

MRN lesioned rats did not differ significantly from the controls, but the DRN lesioned rats showed a profile similar to that seen with anxiolytic drugs (File & Hyde, 1978). Controls in which 6-hydroxydopamine was injected into the DRN showed that this behavioural profile was not due to catecholamine depletion.

Following MRN lesions there was no 5-HT depletion in the caudate, but hippocampal 5-HT concentrations were reduced to 59% of the controls. Following DRN lesions 5-HT was reduced to 65% of the controls in the caudate, and to 44% in the hippocampus. Thus 5-HT lesion of the DRN seems important for producing the anxiolytic profile; whether lesion of the MRN is also necessary cannot be resolved. Seven amino acids were measured by microdansylation (Clark & Collins, 1976). The MRN lesioned rats had significantly raised alanine and

lowered GABA levels compared with controls ($P<0.001$, t-tests); the DRN lesioned rats had no amino acid levels significantly different from controls.

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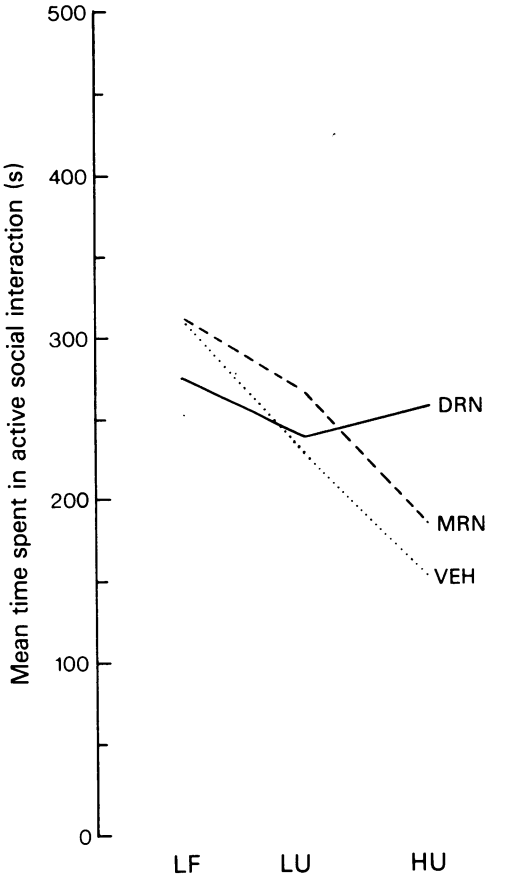

Figure 1. Mean time(s) spent in active social interaction in the low light, familiar (LF), low light, unfamiliar (LU) and high light, unfamiliar (HU), by vehicle controls (VEH), MRN and DRN lesioned rats, Six pairs of rats were tested in each condition, and no pair was tested more than once.

A functional antagonism between benzodiazepines and ACTH?

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Behavioural experiments carried out in this laboratory have implied an anxiety inducing role for ACTH which can be counteracted by chronic treatment with anxiety relieving drugs. Furthermore these experiments have suggested that this interaction involves serotonin containing neurones originating in the Dorsal Raphe Nucleus (Collins, File, Hyde & MacLeod, 1978; File & Vellucci, 1978). It seemed of value therefore to conduct electrophysiological and biochemical experiments in order to assess these interactions in a suitable system at the neuronal level.

Possible ACTH, benzodiazepine, and neurotransmitter interactions were investigated *in vitro* using slices of several limbic areas from the rat brain employing conventional neurochemical techniques (Starr, James & Gaytten, 1978). Flurazepam (FZ; 10^{-7}–10^{-5}M) produced an increase in spontaneous but a decrease in potassium-evoked release of [^{3}H]-5HT from amygdaloid but not hippocampal slices. Although ACTH had no effect on 5HT release, the peptide (10^{-7}-10^{-5}M) antagonized the modulating action of FZ. ACTH and FZ, in the doses used, had no effect on the release of radiolabelled GABA, noradrenaline or acetylcholine.

The spontaneous activity of neurons in the corticomedial region of the amygdala in urethane anaesthetized rats was depressed by the iontophoretic application of γ-aminobutyric acid (GABA) and chlordiazepoxide (CDP). Mixed effects were observed with 5-HT and ACTH but the majority of cells encountered were inhibited by both compounds (87 and 61% respectively). The inhibitions evoked by 5-HT were susceptible to antagonism by ACTH (15 out of 28 tests) and CDP (12 out of 15 tests). Surprisingly,