tions of SP-immunoreactivity in medullary raphe neurones, and distorted, presumably degenerating, axons containing SP in the medulla and spinal cord. Immunohistochemical studies at longer times after 5,6-DHT (up to 20 months) failed to show any reappearance of SP-containing fibres or terminals in areas depleted by the toxin treatment. This suggests that the neurones which may contain both SP and 5-HT represent a separate population of raphe neurones, since other 5-HT cells in the medullary raphe have been shown to sprout extensively after 5,6-DHT and reinnervate many of the denervated areas (Baumgarten, Björklund, Lachenmayer, Rensch & Rosengen, 1974).

The possible descending SP/5-HT system revealed by 5,6-DHT injection may correspond to the pathway known to produce supraspinal analgesia (Basbaum, Clanton & Fields, 1976).

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**Table 1** Effect of 5, 6-DHT on substance P content of medulla and spinal cord

| | *Substance P content (ng/g protein)* | | |
|---|---|---|---|
| *Region* | *Control* | *2 weeks* | *20 months* |
| Medullary raphe | 699 ± 56 (3) | *440 ± 67 (3) (−37%) | 703 ± 128 (4) (+0.6%) |
| Dorsal cervical Spinal cord | 3109 ± 292 | *1675 ± 192 (3) (−46%) | *1261 ± 281 (4) (−59%) |
| Ventral cervical Spinal cord | 802 ± 161 (3) | 693 ± 63 (3) (−14%) | *427 ± 88 (4) (−47%) |
| Dorsal lumbar Spinal cord | 2909 ± 110 (3) | 2148 ± 764 (3) (−26%) | *1604 ± 109 (4) (−45%) |
| Ventral lumbar Spinal cord | 704 ± 48 (3) | *49 ± 45 (3) (−93%) | *62 ± 19 (4) (−91%) |

SP contents of tissue samples were measured by a radioimmunoassay (Kanazawa & Jessell, 1976).
Values in brackets represent numbers of animals used for each determination, and percentage change in SP levels from control.
*Denotes $P<0.05$ by Students $t$-test.

## Dose dependent behavioural stimulation after local infusion of substance P into the ventral tegmental area in the rat


SUSAN D. IVERSEN, ANN E. KELLEY & L. STINUS

*Psychological Laboratory, University of Cambridge, Downing Street, Cambridge*


Evidence is accumulating that the polypeptide substance P (SP) is an excitatory neurotransmitter in the mammalian CNS. Regional distribution studies have revealed that particularly high concentrations of SP are found in the ventral mesencephalon. One SP-containing pathway which has been described in detail originates in the medial habenula and innervates the ventral tegmental area (VTA) (Cuello, Emson, Paxinos & Jessell, 1978). The VTA contains the dopaminergic A 10 (DA-A10) cell bodies which form

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


G.G.S. COLLINS, SANDRA E. FILE, J.R.G. HYDE & N.K. MACLEOD

*Department of Pharmacology, The School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX*


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