Behavioural Brain Research, 56 (1993) 197–201

BBR 01473

Short Communication

Haloperidol exaggerates proprioceptive-tactile support reflexes and diminishes vestibular dominance over them

Alan J. Cordover, Sergio M. Pellis and Philip Teitelbaum

Department of Psychology, University of Florida, Gainesville, FL 32611 (USA)

(Received 27 August 1991)
(Revised version received 16 April 1993)
(Accepted 12 May 1993)

Key words: Catalepsy; Dopamine; Righting; Postural support; Rat

Rats made immobile and cataleptic by haloperidol, a dopamine receptor blocker, maintain their static stable equilibrium by employing a variety of allied postural support reflexes. Under some test conditions, competition between such reflexes occurs, and in haloperidol-treated rats, unlike undrugged controls, proprioceptive-tactile stimuli appear to be dominant over vestibular stimuli. We investigated this relationship in rats by testing their air-righting with and without simultaneous contact of the tail on a wooden platform. The rats were lightly held in a supine position by the shoulders and pelvis, with or without tail contact on a small wooden platform 47 cm above the ground. Undrugged rats showed the normal pattern of righting which involves axial rotation with cephalocaudal recruitment whether the tail is contacting the platform or not. Upon release, the haloperidol-treated rats (2.5 mg/kg) gripped the platform with their tail, which interfered with the air-righting reflex. This demonstrates that in haloperidol-treated rats, the dominance of tactile-proprioceptive postural support reflexes over those triggered vestibularly.

Dopaminergic depletion or blockade of the dorsal striatum produces a state of akinesia and catalepsy[5,13,16]. That is, the subject not only remains unmoving, but will actively defend its static stable equilibrium[5,15,19]. To do so, the subject uses a variety of postural support reflexes either to maintain stability (e.g. bracing and clinging), or regain stability (e.g. righting)[5,10]. Due to this exaggerated maintenance of postural stability and the absence of locomotion, cataleptic subjects maintain awkward postures, such as clinging to a vertical grid[6]. Such catalepsy can be effectively produced in rats by the injection of low to moderate doses of neuroleptics, such as haloperidol[3,5]. The cataleptic rat provides a useful subject for the study of postural support reflexes, since other behaviors that may interfere are inhibited[19]. Using this approach, specific postural support reflexes can be isolated (e.g. bracing, clinging, righting), thus enabling the analysis of their subcomponent responses and their interaction[5,8,10,12]. In addition, interactions among different postural support reflexes can be studied[14].

Schallert and Teitelbaum[14] showed that when rats are given a wire mesh grid to grasp and cling to, and are dropped from a supine position, they will maintain their grip on the grid, rather than right. In undrugged rats, this effect was difficult to obtain. It appeared that they had more variable movements that were not directly related to maintaining static stable equilibrium. Nonetheless, under the right stimulus conditions, intact rats also showed this dominance of clinging over righting[14]. By inhibiting movements unrelated to postural support, haloperidol-induced catalepsy made this interaction between clinging and righting readily testable. However, because of the nature of the experiment, and the body parts used in the responses, this experiment was unable to identify the underlying neural mechanism.

Clinging inhibits vestibular righting only if the forepaws are gripping, and only if the grids for each paw are connected to one another. As the rats fall, they tighten their grip and flex their forelimbs, making the grid, paws, limbs and shoulders a single unit[14]. In rats, righting is initiated by the shoulders, which passively carries the head and neck to prone[5,9]. When clinging, the tight grip and the associated ventroflexion of the upper torso may be in competition with this rotation. That is, the "one body unit" cannot perform two different movements simultaneously. Therefore, the clinging response may out-compete the rotation response. Another example of this competition is illustrated in the ventroflexion preceding rotation in both intact and

Correspondence: S.M. Pellis, Department of Psychology, University of Lethbridge, Lethbridge, Alberta T1K 3M4, Canada.

haloperidol-treated rats when rats fall supine in the air[5,9,10]. If the ventroflexion is exaggerated and persists, rotation does not occur[17]. With the available evidence, it is not possible to determine whether clinging neurally inhibits vestibular righting, or whether there is a failure to inhibit clinging, which is necessary to permit righting to occur. In either case, clinging would be antagonistic to righting, but the underlying physiological mechanism would be quite different.

During our studies on the role of vision in modulating air-righting[9,11], we discovered that contact of the tail with the ground, like paw contact with the grid[14], interferes with normal vestibular righting. However, since in this case the site of movement for the two responses is different (tail versus shoulders), the issue of whether there is proprioceptive-tactile inhibition of vestibular righting can be addressed.

Fifteen male Long–Evans hooded rats weighing between 326 and 470 g were used. The animals were housed individually in wire-mesh hanging cages in a temperature controlled room at 21–23 °C on a 12:12 h light/dark cycle, lights on at 07.00 h. Each of the first nine rats tested were injected intraperitoneally (i.p.) with saline. Approximately 45 min later, the rats were tested behaviorally. Three to five days later, they were injected i.p. with 2.5 mg/kg of haloperidol, and were also tested after 45 min. To test their air-righting, they were dropped supine 10 times from a height of approximately 47 cm onto a 10 cm thick foam cushion. The rats were not released until they had ceased struggling and were relaxed in the experimenter's fingers[9,11]. They were dropped with their tail in contact with a wooden plank that was also elevated 47 cm above the ground by a metal rod (see Figs. 1 and 2). The righting trials were recorded using a Panasonic (WV-D5000) strobe video camera, with a strobe effect shutter having a speed of 1/1000 s for exposure every 1/60 s. This provided high resolution blur-free frames for analysis of the movement at a speed of 30 frames/s.

Whether dropped with or without the tail in contact with the elevated platform, the rats injected with saline righted normally. That is, there was a short delay upon release, and then the rat's body rotated around the longitudinal axis; first with the shoulders, and then with the pelvis (Fig. 1). In this way, the animal landed on the ground prone, facing the same direction as when it was held supine in the air. The latency was scored from the first videoframe of release to the first frame when the shoulders began to rotate around the longitudinal body axis, as well as the latency from the first frame of shoulder rotation to the first frame of pelvic rotation, for trials without and with contact with the platform. In the saline-treated rats, tail contact did not change the la-

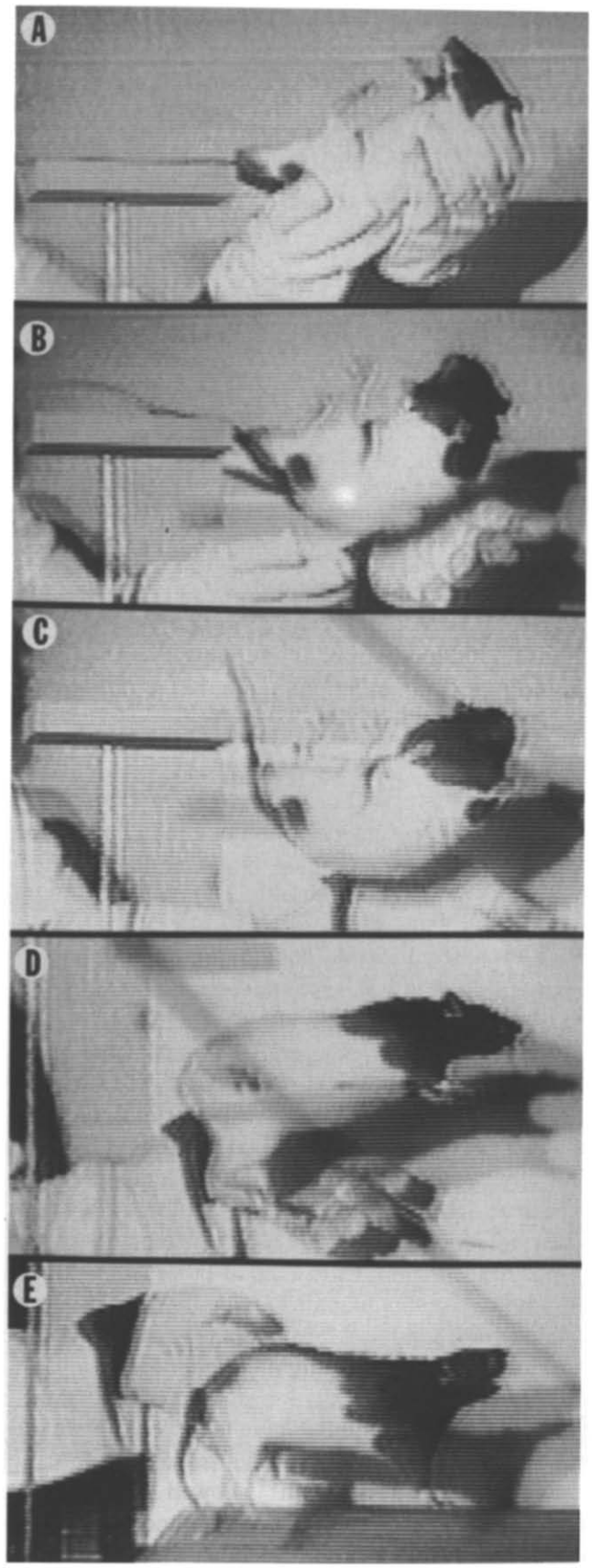
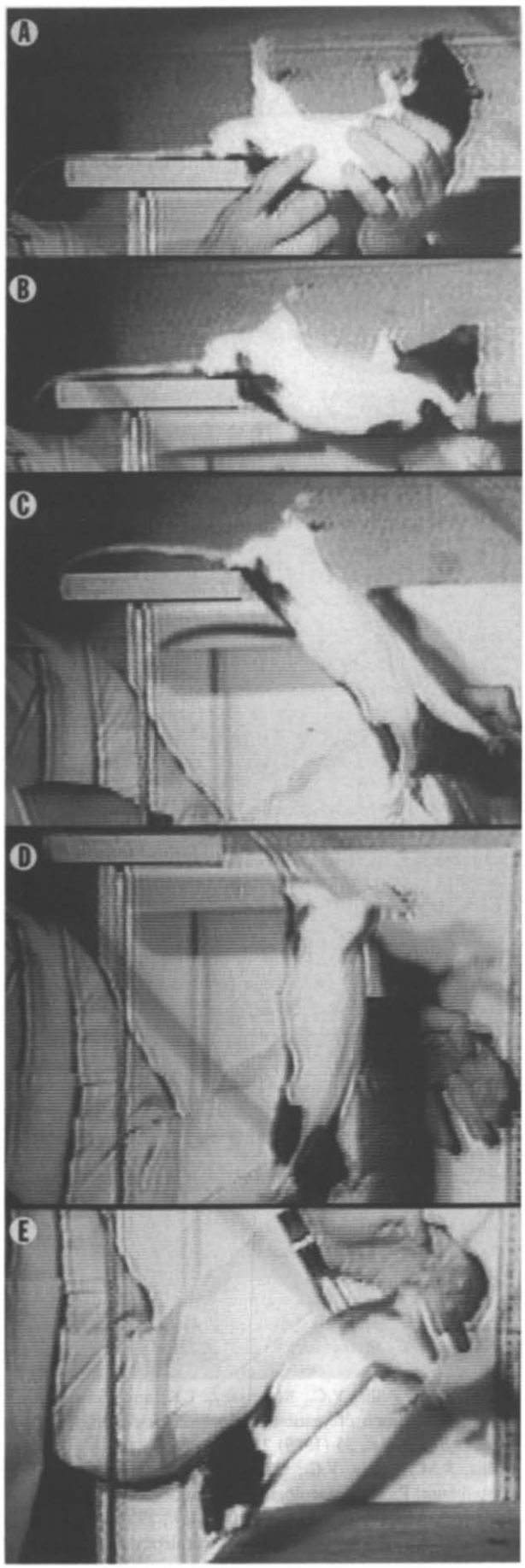


Fig. 1. A saline-treated rat, with full tail contact, rights in the normal cephalocaudal sequence. (Photographs taken from videoscreen.)



tency of initiating shoulder rotation ($\bar{x} \pm$ S.E.: 57.2 ± 8.6 ms vs. 59.8 ± 8.7 ms) or pelvis rotation (40.2 ± 8.3 ms vs. 30.6 ± 16.4 ms). Without tail contact on the platform, rats treated with haloperidol righted in the same manner (see also refs. 5, 9).

With tail contact, haloperidol-treated rats righted in a different manner. Upon release, the tail gripped the wooden platform, delaying the onset of rotation of both the shoulders (47.9 ± 12.3 ms vs. 78.6 ± 6.2 ms; $t = 7.14$, df = 8, $P < 0.001$) and the pelvis (49.7 ± 8.5 ms vs. 73.6 ± 9.3 ms; $t = 5.38$, df = 8, $P < 0.001$). Because the tail anchored the hindquarters, the rat's forequarters fell downward faster than the hindquarters, so that upon landing prone, the longitudinal axis faced 180 degrees in the opposite direction to which they were dropped. As shown in Fig. 2, the rats were held supine facing the right side of the page but landed prone facing the left side. Even though shoulder rotation was delayed by the presence of tail contact, the shoulders nonetheless did rotate 45–90 degrees (Fig. 2B). In contrast, in 67 cases, where the position of the tail could be scored, it was found that the pelvis was recruited to rotate in the direction of the shoulders only when the tail lost contact with the platform. Indeed, if the body was perpendicular to the ground at this point (Fig. 2C), then the pelvis remained unmoving, and the shoulders rotated back around the longitudinal axis towards the pelvis, so that the shoulders and the pelvis were again in alignment when landing prone (Fig. 2 D,E). In undrugged rats, the gripping by the tail was only observed when they were struggling. If the rats were dropped while struggling, they tightened their tail grip, and by doing so, flipped around in the air (as in Fig. 2). If the rats were relaxed prior to dropping, this did not occur. It appears then, that the use of the tail as a 'fifth limb' is exaggerated in cataleptic rats[2], and that the gripping becomes the dominant response when dropped supine with tail contact.

To control for an order effect, an additional six rats were also tested; but this time, three rats were tested first with haloperidol and then with saline, and the other three in reverse order. Each rat was rated on a scale which represented the orientation of the head and body when they landed. A score of 0 was given when the rats landed horizontally facing the same direction as when released in the air (as in Fig. 1). A score of 2 was given

Fig. 2. A haloperidol-treated rat, with rump and full tail contact, has an altered pattern of cephalocaudal righting so that it lands facing the opposite direction from which it was released. Note that the additional rump contact present in this example was not necessary to produce the altered pattern of righting. Tail contact, which enabled gripping of the platform was sufficient. (Photographs taken from videoscreen.)

when the rats landed horizontally facing the opposite direction to that when released (as in Fig. 2). If the rats landed head down, perpendicular to the ground, they were given a score of 1. On this scale, 0 represented the absence of tail gripping, and 2 represented strong gripping by the tail. When treated with haloperidol, the rats were more likely to grip with the tail ($\bar{x} \pm$ S.E.: 1.61 ± 0.05), compared to when treated with saline (0.09 ± 0.03) (Wilcoxon matched pairs signed ranks test: $t = 0$, $n = 6$, $P < 0.05$). Similarly, when tested with tail contact, the delay in the onset of shoulder rotation tended to be longer when treated with haloperidol. The absolute difference in time to initiate forequarter rotation between free fall trials and trials with tail contact when injected with saline and with haloperidol was calculated. The difference tended to be greater when the rats were treated with haloperidol (31.33 ± 6.00 ms vs. 13.00 ± 3.33 ms), although due to the sample size and variance the difference was not significant ($t = 1.84$, df = 5, $P > 0.05$).

These findings suggest that gripping and righting are antagonistic to one another, as previously shown by Schallert and Teitelbaum[14] for forepaw clinging and righting. Furthermore, in the present case, clinging by the tail rather than by the forelimbs clearly shows that, in part, this antagonism involves an inhibitory relationship of the tactile-proprioceptive over vestibular systems. After all, clinging by the tail does not physically preclude rotation by the shoulders, as may be the case for forelimb clinging. Indeed, after an haloperidol-induced delay, the shoulders do rotate, but while the tail is maintaining contact with the platform, the rats fail to recruit the pelvis. Since recruitment of the pelvis following rotation of the shoulders during righting involves a proprioceptive signal from the vertebral column[7], this suggests that the tail contact is also inhibiting the non-vestibular phase of righting. This further also suggests that contact with the tail generally inhibits righting, and not only vestibular righting.

Bandaging the head or body, or clamping the skin (especially at the nape) can inhibit a number of postural support reflexes, including forepaw gripping[5,12,18] and righting in the air[1] and on the ground[4,10]. In all these cases, however, these effects are either more pronounced or not present unless the rats are cataleptic. For example, an undrugged labyrinthectomized rat that has been placed supine with a piece of plexiglass pressed against its palms will not only remain supine, but will even "walk" and "explore"[1], whereas an intact rat will immediately right itself. However, an intact, haloperidol-treated rat, will, like the undrugged labyrinthectomized rat, remain inverted as long as the the plexiglass contact on the palmar surface is maintained (Pellis and Teitelbaum, unpublished observations). These observations indicate the possibility that in the cataleptic state, not only has the relative dominance of tactile over vestibular responses changed, but also the dominance of some tactile signals over others (i.e. palm over the dorsal surface of the body). In this way, gripping with the tail or paws signals support; and these signals of support are dominant over postural support reflexes, be they vestibular or tactile-proprioceptive.

ACKNOWLEDGEMENTS

We wish to thank V. Pellis for help in the laboratory and for her helpful comments, as well as those of the reviewers, and A. Allen for typing the paper. This work was supported by a Whitehall Foundation grant to P. Teitelbaum.

REFERENCES

1 Chen, Y.-c., Pellis, S.M., Sirkin, D.W., Potegal, M. and Teitelbaum, P., Bandage backfall: labyrinthine and non-labyrinthine components, *Physiol. Behav.*, 37 (1986) 805–814.
2 Cole, J. and Dearnely, D.P., Contrasting tail and other responses to morphine and reserpine in rats and mice, *Experentia*, 16 (1959) 78–80.
3 Costall, B. and Naylor, R.J., On catalepsy and catatonia and the predictability of the catalepsy test for neurologic ability, *Psychopharmacologia*, 34 (1974) 233–241.
4 De La Cruz, F., Junquera, J. and Russek, M., Ontogeny of immobility reactions elicited by clamping, bandaging, and maternal transport in rats, *Exp. Neurol.*, 97 (1987) 315–326.
5 DeRyck, M., Schallert, T. and Teitelbaum, P., Morphine versus haloperidol catalepsy in the rat: a behavioral analysis of postural mechanisms, *Brain Res.*, 201 (1980) 143–172.
6 Fog, R., On stereotypy and catalepsy: Studies on the effects of amphetamines and neuroleptics on rats, *Acta Neurol. Scand.*, 50 (1972) 1–66.
7 Magnus, R., *Korperstellung*, Springer, Berlin, 1924. (A 1987 English translation of *Body Posture* is available from the U.S. Department of Commerce.)
8 Pellis, S.M., Chen, Y.-c. and Teitelbaum, P., Fractionation of the cataleptic bracing response, *Physiol. Behav.*, 34 (1985) 815–823.
9 Pellis, S.M., Pellis, V.C. and Teitelbaum, P., Air righting without cervical righting reflex in adult rats, *Behav. Brain Res.*, 45 (1991) 185–188.
10 Pellis, S.M., De La Cruz, F., Pellis, V.C. and Teitelbaum, P., Morphine subtracts subcomponents of haloperidol-treated postural support reflexes revealing gradients of their integration, *Behav. Neurosci.*, 100 (1986) 631–646.
11 Pellis, S.M., Pellis, V.C., Morrissey, T.K. and Teitelbaum, P., Visual modulation of vestibular-triggered air-righting in the rat, *Behav. Brain Res.*, 35 (1989) 23–26.
12 Pellis, S.M., Pellils, V.C., O'Brien, D.P., De La Cruz, F. and Teitelbaum, P., Pharmacological subtraction of the sensory controls over grasping in rats, *Physiol. Behav.*, 39 (1987) 127–133.
13 Sanberg, P., Haloperidol-induced catalepsy is mediated by

postsynaptic dopamine receptors, *Nature*, 284 (1980) 472–473.
14 Schallert, T. and Teitelbaum, P., Haloperidol, catalepsy and equilibrating functions in the rat: antagonistic interaction of clinging and labyrinthine righting reactions, *Physiol. Behav.*, 27 (1981) 1077–1083.
15 Schallert, T., Whishaw, I.Q., DeRyck, M. and Teitelbaum, P., The postures of catecholamine-depletion catalepsy: Their possible adaptive value in thermoregulation, *Physiol. Behav.*, 21 (1978) 810–817.
16 Schallert, T., DeRyck, M., Whishaw, I.Q., Ramirez, V.D. and Teitelbaum, P., Excessive bracing reactions and their control by atropine and L-Dopa in an animal analog of Parkinsonism, *Exp. Neurol.*, 64 (1979) 33–43.
17 Sirkin, D.W., Schallert, T. and Teitelbaum, P., Involvement of the pontine reticular formation in head movements and labyrinthine righting in the rat, *Exp. Neurol.*, 69 (1980) 435–457.
18 Teitelbaum, P., Wolgin, D.L., DeRyck, M. and Marin, O.S.M., Bandage-backfall reaction: occurs in infancy, hypothalamic damage, and catalepsy, *Proc. Natl. Acad. Sci. USA*, 73 (1976) 3311–3314.
19 Teitelbaum, P., Schallert, T., DeRyck, M., Whishaw, I.Q. and Golani, I., Motor subsystems in motivated behavior. In R.F. Thompson, L.H. Hicks and V.B. Shvyrkov (Eds.), *Neural Mechanisms of Goal-Directed Behavior and Learning*, Academic Press, New York, 1980, pp. 127–143.