

Why do we have a caudate nucleus?

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In order to understand the physiological role of the caudate nucleus, we combine here our laboratory data on cats with reports of patients with selective damage to this nucleus. Cats with bilateral removal of the caudate nuclei showed a stereotyped behavior consisting of persistently approaching and then following a person, another cat, or any object, and attempting to contact the target. Simultaneously, the animals exhibited a friendly disposition and persistent docility together with purring and forelimbs treading/kneading. The magnitude and duration of this behavior was proportional to the extent of the removal reaching a maximum after ablations of 65% or more of the caudate tissue. These cats were hyperactive but they had lost the feline elegance of movements. Additional features of acaudate cats were: (1) postural and accuracy deficits (plus perseveration) in paw usage tasks including bar pressing for food reward; (2) cognitive and perceptual impairments on a T-maze battery of tasks and on the bar pressing tasks; (3) blockage or blunting of the species-specific behavioral response to a single injection of morphine; Unilateral caudate nucleus removal did not produce global behavioral effects, but only deficit in the contralateral paw contact placing reaction and paw usage/bar pressing. Moreover and surprisingly, we found hypertrophy of the ipsilateral caudate nucleus following prenatal focal neocortical removal. The findings in human were also behavioral (not neurological) and also occurred with unilateral caudate damage. The main manifestations consisted of loss of drive (apathy), obsessive-compulsive behavior, cognitive deficits, stimulus-bound perseverative behavior, and hyperactivity. Based on all of the above data we propose that the specific function of the caudate nucleus is to control approach-attachment behavior, ranging from plain approach to a target, to romantic love. This putative function would account well for the caudate involvement in the pathophysiology of a number of clinical syndromes that we mention, all of which compromise approach-attachment- affect behaviors. In addition we conclude that the caudate nucleus contributes importantly to body and limbs posture as well as to the accuracy and speed of directed movements.

Key words: caudate nucleus, functional role, consequences of removal, behavior, cats, humans

INTRODUCTION

The functional role of the caudate nucleus (CdN) is generally described in the context of the neuroanatomical and functional basal ganglia “loops” to which it belongs, or as the structure which initiates the direct and indirect pathways of the basal ganglia. In contrast, the purpose of this review is to show that the Cd has a function of its own, independently of the neural networks in which this large nucleus (n.) is imbedded. We have not found any recent review with this particular focus.

Starting in 1975 (Villablanca et al. 1976a) we embarked in a long series of studies to analyze the behavioral effects of bilateral removal of the CdN in cats (and latter on, in kittens). A review of these studies up to 1982 was published in this Journal (Villablanca and Olmstead 1982), but our work on this field continued intermittently and expanded to include non-behavioral work as well (e.g., Loopuijt and Villablanca 1993). In the Discussion section of our 1982 paper, we highlighted the fact that we had not found reports of human studies up to that time-point and suggested that such studies were sorely needed. We noted, furthermore, that Cd lesions could now be documented using the emerging radiological imaging techniques. A number of studies in patients have been reported (e.g., Kailash and Marsden 1994) since then and are available for comparisons to our studies in cats.

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In the first section of this paper, we review our results in cats with bilateral removal of the Cd, or acaudate cats. In the second section, we describe and discuss the reported effects of Cd nuclei damage in humans and relate these findings to the results in cats. Other, non-behavioral, relevant findings in cats are mentioned in a third section. Finally, in the Conclusion section we attempt to combine all findings to propose an answer to the question raised in the title of this paper. In all our experiments reviewed here efforts were made to minimize suffering and to use a minimal number of animals. All procedures were approved by the UCLA Chancellor's Committee on Animal Research.

Clinical syndromes in which the CdN is involved will be mentioned, but we wish to emphasize that it is beyond the purpose of this review to discuss the pathophysiological role of the CdN in these conditions.

In terms of anatomical connectivity and very briefly, the largest contingent of afferent fibers to the CdN come directly from all areas of the neocortex, with only about 10% of the terminals arriving from the s. nigra pars compacta (Hokfelt and Ungerstedt 1969). Other projections arrive from the thalamus, raphe nuclei, and amygdala. In turn, the CdN projects back only to the frontal cortex (via the thalamus) and, downstream, it projects to the globus pallidus, thalamus, and s. nigra pars reticulata. For details, see any recent neuroanatomy/neuroscience book.

THE CAT WITHOUT CAUDATE NUCLEI

Contrary to predictions from the literature that animals without the CdN can not be maintained alive (e.g., Mettler and Mettler 1942, Harik and Morris 1973), we were able to prepare cats (Villablanca et al. 1976a) and kittens (Villablanca et al. 1978) with up to complete removal of the Cd nuclei. The removal was selective because we used a midline cortex transcallosal surgical approach; i.e., with a thin suction pipette we penetrated the lateral ventricle through a small opening in the gyrus cinguli and subsequent perforation of the corpus callosum, thereby sparing the dorso-lateral neocortex. In the rat corticofugal nerve fibers crossing the Cd are abundant while, in contrast, nerve fibers are rare in the Cd of the cat and, consequently, damage to fibers of passage was essentially avoided. In addition, due to the soft consistency of the CdN, we

were able to use a low suction strength, and this greatly helped to keep to a minimum the damage to adjacent structures. The amount of the removal was calculated for each brain by reconstructing the ablation on 5 anterior-posterior planes of the atlas by Snider and Niemer (1961). Thereafter, a grid consisting of 10 mm squares was superimposed over each of the 5 mentioned planes of the atlas and the number of grid squares covered by each corresponding ablation area was calculated. This allowed us to compute a numerical index and to then calculate the amount of Cd removed. A representative example of the ablation at the level of 4 A-P planes is shown in Fig. 1. The putamen was spared; however, this structure is relatively small in cats (about one fifth of the Cd volume; Loopuijt and Villablanca 1997) and, furthermore, no additional effects were seen in a few animals in which a putamen lesion was added to the Cd removal. Over 30 adult cats and 17 kittens with up to a 100% bilateral removal of the Cd – to be called acaudate cats – were maintained indefinitely together with comparison animals with unilateral Cd removal or bilateral frontal cortex ablation, as well as a number of “control” cats (see below and Villablanca et al. 1976a).

The key behavioral change following bilateral Cd removal was a profound and impressive shift from the typical feline aloofness of cats to an opposite type of behavior which we have called “compulsory approaching syndrome” or CAs (Villablanca et al. 1976a). This consisted of the cat approaching and then following a moving person (Fig. 2A), another cat (Fig. 2B), or any object in a stereotyped manner and with a strong tendency to contact the target. Stimuli other than visual also elicited this behavior; e.g., a sudden noise would distract/redirect a visually approaching cat. All of this within a background of motor hyperactivity (restlessness and persistent wandering/exploring around in the lab). This was not a purely motor behavior event since it was regularly associated to other changes best described as pertaining to the realm of affect or “mood” (Villablanca et al. 1976a, Villablanca and Olmstead 1982). The cats exhibited marked docility and a friendly disposition, persistent purring, repetitive treading or kneading of the forelimbs (Fig. 2D), and the rooting response (Fig. 2C; Villablanca et al. 1976a). Interestingly, male acaudate cats exhibited the typical female lordotic sexual behavior when touching their back at the lumbar spine level; however, and as reported in (Olmstead et al. 1982), this was not due to

any hormonal changes. The CAs was a stereotyped behavior which was never present during the presurgical testing of the cats. Furthermore, the magnitude and duration of this syndrome was correlated with the amount of caudate tissue removed. In animals with 65% or more of Cd tissue destroyed the CAs was maximal and lasted indefinitely (Villablanca et al. 1976a, Villablanca and Olmstead 1982).

Since the Cd nuclei and the frontal cortex may share some functions, the most important comparison group consisted of cats with bilateral ablation of the frontal

cortex (removal of tissue in front of a coronal line equidistant from the cruciate and ansatus sulci), to be called afrontal cats. In contrast with the acaudates, these cats were generally timid and tended to run away and hide. Only about 19% of them showed some aspects of the CAs but lasting no longer than 2–4 weeks post ablation.

None of the acaudate cats showed any gross neurological abnormality (e.g., tremor, rigidity, abnormal movements), and this was surprising. Others have reported athetoid/choreiform movements in cats with

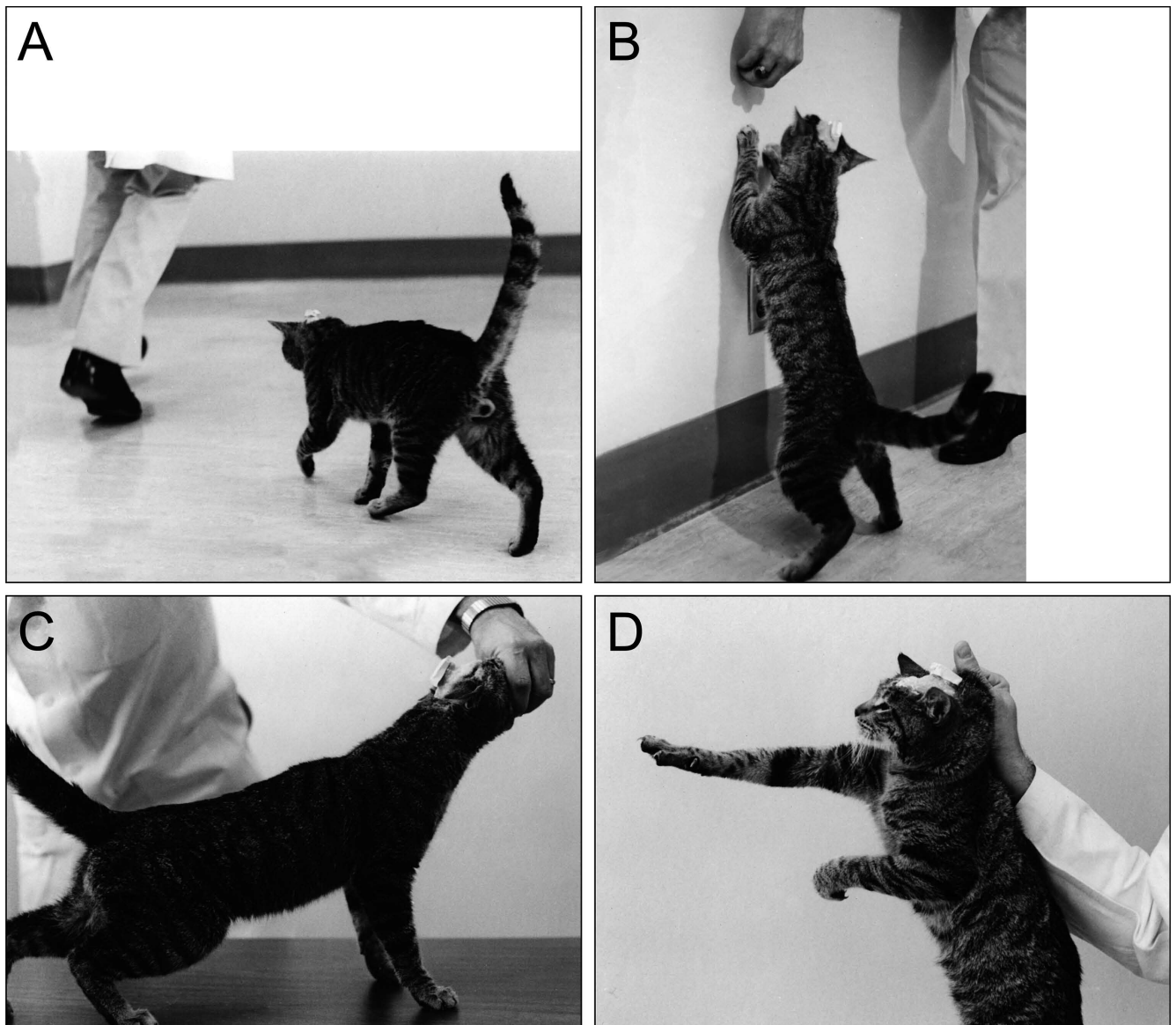


Fig. 1. Still camera pictures showing a cat with bilateral removal of the caudate nuclei. (A) Compulsively following a person; (B) attempting to climb up a wall to approach the investigator's hand; (C) displaying the rooting behavior; (D) performing stereotyped treading movements of the forelimbs. Reprinted from Villablanca and Olmstead 1982 [with permission from *Acta Neurobiol Exp (Wars)*].

lesions much smaller than ours (Liles and Davis 1969, Sanders et al. 1975). However, as we have pointed out (Villablanca et al. 1976a), the description of these movements fits indeed the appearance of the exaggerated treading/kneading paw movements that we see as an integral part of the CAs. Overall, acaudate cats impressed as slow and impoverished in their ordinary motor activities, in contrast with the typical feline elegance and graceful movements of normal cats, and this was certainly reminiscent of hypokinesia and bradykinesia, as was also seen in some of the performance tests described below.

We also studied cats with unilateral removal of the CdN (Villablanca et al. 1976a). These animals tended to turn/walk ipsilaterally to the removal for 1–2 days after the ablation, but none of the manifestations following bilateral ablation were ever seen in these cats.

Other findings in acaudate cats will be summarily described below.

Sleep-waking patterns and spontaneous motor activity were also evaluated. For this purpose we conducted and analyzed 24 h polygraphic recording sessions starting on the 5th post-ablation day and repeated every 10–15 days (first 3 months) and 10–30 days thereafter for up to 6 months (Villablanca et al. 1976b). Waking significantly increased during this period, from 37.9% of recording time in control cats to 58.2% in acaudates, while REM sleep decreased from 15.5% in control cats to 10.8% in acaudates. Once again, however, afrontal cats also showed hypsomnia. Motor activity increased markedly with a larger increase for the acaudate cats (68%) compared to the afrontal (55%); These results were confirmed in Open Field testing experiments (Levine et al. 1978).

The contact placing reaction (CP) of the limbs was lost in cats sustaining an ablation greater than 65% of the CdN (Villablanca et al. 1976c). This is a delicate response consisting of an automatic replacement of the limb when the paw falls off a surface. It has been traditionally accepted that this reaction depends on the integrity of the motor cortex (Bard 1933). However, due to the extent of the loss in adult acaudates and because in acaudate kittens the impairment was even greater than following frontal cortex removal (Villablanca et al. 1978), we have proposed that the Cd is an integral component of the CP physiological mechanism.

The acaudate cats had typical deficits in a paw usage task consisting of reaching for morsels of meat

placed on a tray running in front of a testing box, and through a narrow opening under a transparent door (Olmstead and Villablanca 1979). The paw movements were posturally abnormal, inaccurate, as well as perseverative. The paw posture was closer to normal in afrontal cats, but these animals showed, in contrast to acaudates, an inconsistent and unmotivated performance.

Acaudate cats showed a number of deficits on a bar pressing (BP) battery of tasks (using a Skinner testing box), and only 1 of 3 cats with ablations greater than 60% could learn how to BP (Olmstead et al. 1976). Moreover, only cats with the smaller removals (about 30% of the CdN), were able to perform single alternation (switching each trial between the left and the right bars). The main problems were: (1) delay in initiating performance (akinesia?); (2) the need to shift the body position, each trial, to the side of the bar to be pressed while intact cats stayed in the midline of the bar pressing box (Fig. 3); (3) slowness of movements and performance (bradykinesia?); (4) inability to BP and drink the milk reward simultaneously (asynkinesia?); (5) inability to perform single alternation; and (6) perseverative behavior. The afrontal cats were hard to motivate to perform, and showed irregular and slow performance.

A T-maze battery of tasks highlighted the cognitive and perceptual impairments of acaudate cats (Olmstead et al. 1976). Acaudate cats, as expected, took significantly fewer trials than the other groups to learn making five consecutive responses to the rewarded side of the maze. However, when the locus of reinforcement was reversed, perseveration prevented acaudates learning to switch the initial position habit and, consequently, they produced significantly more errors than the other animal groups (Fig. 4). For the next stage of the task, the door of the start box of the maze was painted black on one side and white on the other. It was clear that the acaudates could discriminate colors, however, significantly fewer of them reached discrimination criterion compared to the other groups and those that did, took significantly more trials. Moreover, when the location of the food reward was switched to the opposite side than that formerly learned (discrimination reversal), the task was impossible for the acaudate cats to master. Once again, the degree of the impairment was proportional to the amount of Cd tissue removed. The afrontal cats showed no statistical differences compared to the intact cats, however, as for the bar press-

ing task, their performance was irregular, unmotivated, and unsustained.

A passive avoidance task showed that the CAs was not a consequence of acaudate cats inability to perceive and avoid a threat. After one trial these cats learned (and retained the learning) not to step down from a safe platform into a floor of brass rods where they would get a mild electric shock (Olmstead and Villablanca 1980).

On a test of behavioral reactivity to auditory stimuli (tones and cat vocalizations taped in our kitten colony), the most responsive cats were the adult acaudates (Villablanca et al. 1978) since their level of responsiveness persisted over the 50% level (relative to intact cats) across the 3 sessions of the test. Afrontal cats were hyperresponsive also, but at a significantly

lower level than the acaudates.

The complex and stereotypical behavioral response to a single low dose of morphine of intact cats (Villablanca et al. 1982) was cancelled/reduced in the acaudates. In intact cats a small dose of morphine (0.5–3.0 mg/kg) induces a stereotypic, naloxone-sensitive, dose-dependent response with the main behavioral events starting 15–45 min postinjection. These consist of the cat displaying, usually in a sitting position, abundant, discrete, head and paw movements reminiscent of the animal visually following an object in an unpredictable trajectory while at the same time using the paws as for catching an imaginary object. This behavior continues, also in a dose-dependent manner, for up to 5 h. In the acaudate cats this rich behavioral display was attenuated and this reduction

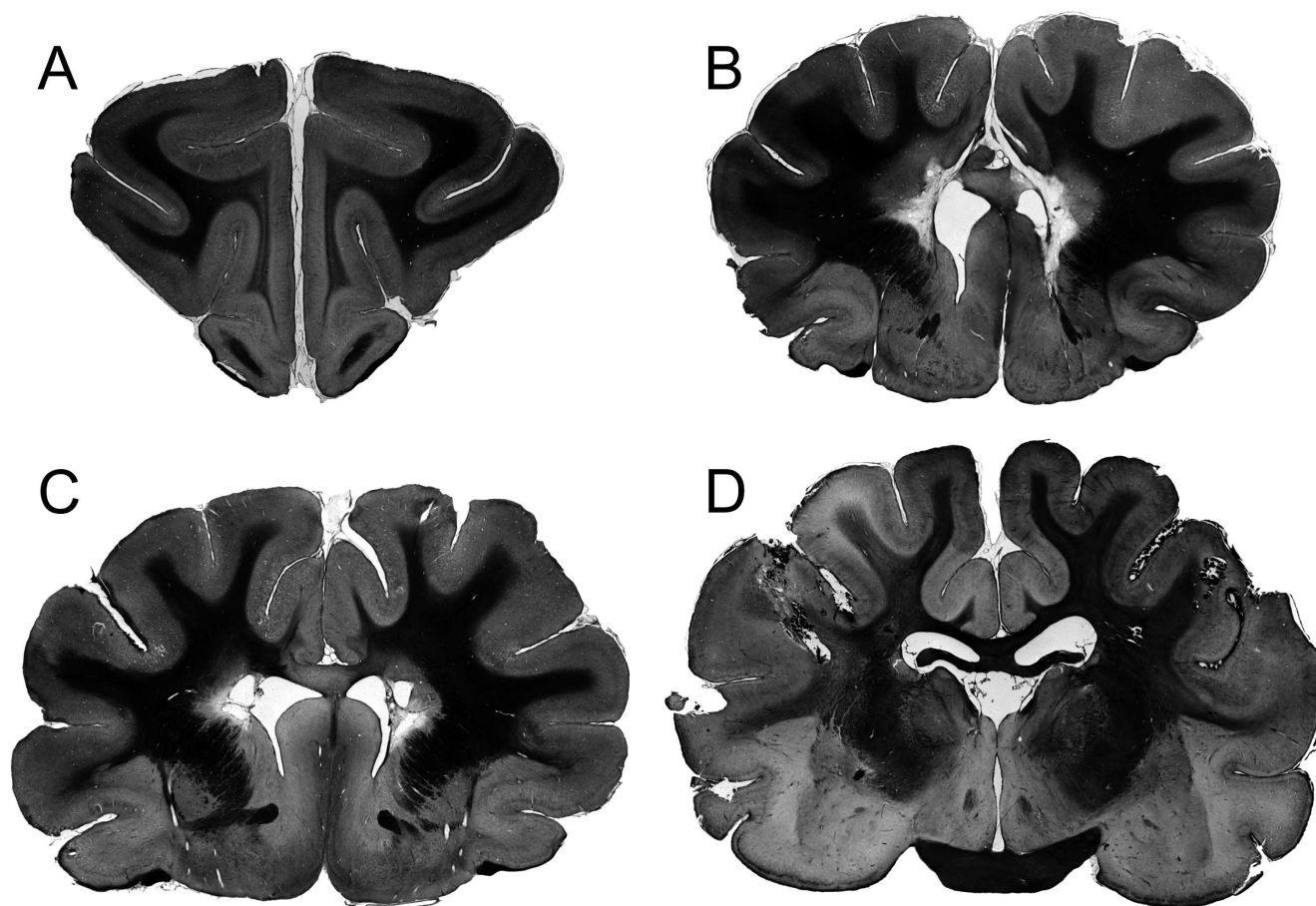


Fig. 2. Coronal sections (Weil stained) of the brain of a cat with unilateral (left side) removal of the caudate nucleus. Section (A) is at frontal level and, together with the removal and cortical surgical penetration site, shows the integrity of the right caudate (as well as the bilateral integrity of the frontal areas); (B) is at the level of the head of the caudate, while (C), and (D), are at the level of the body and the tail of the caudate nucleus, respectively. Note the sparing of the thalamus and of the internal capsule. We decided to show an unilateral removal because it allows to highlight and contrast the absence of the nucleus with the intact and large caudate nucleus that cats possess. Reprinted from Villablanca and Olmstead 1982 [with permission from *Acta Neurobiol Exp* (Wars)].

was proportional to the amount of caudate tissue destroyed. In the cats with the largest ablation it was replaced by an unspecific behavior: the cats showed a progressive increase in walking such that by post-injection hrs 2 to 4 the acaudates with the larger ablations were walking about 60% of the time, which often induced tachypnea and hyperthermia. In a surprising contrast, afrontal cats reacted to morphine injection as intact cats did.

In maturing kittens, the behavioral response to morphine just described begins to emerge (Burgess and Villablanca 2007) only by postnatal day (P) 30 and the process is completed only between P90 and P120. By P30 the CdN is growing and, volumetrically, it reaches adult size only by P45 (Villablanca et al. 2000). Therefore, we believe that the ontogenesis of the response to a single dose of morphine as well as the dependency of this behavioral reaction on the gross anatomical integrity of the CdN, indicate that the Cd mediates the behavioral response to morphine in cats.

To sum up: there was a clear and strong disassociation between the effects of removal of the CdN and of the frontal cortex which points to a specific, unique role of the neostriatum on behavior (the similarities of lesion effects upon motor activity/sleepwaking are non specific, as we have argued in our S-W review, Villablanca 2004).

OTHER FINDINGS IN CATS

The volume of the CdN increases unilaterally following resection of the ipsilateral frontal cortex during fetal life (Villablanca et al. 1993); but the packing density of neuronal and glial cells does not change suggesting a true and exceptional post-lesion hypertrophy (Loopuijt and Villablanca 1993). This hypertrophy did not occur when a similar resection was carried out in adulthood. On the contrary, following the removal of the entire neocortex of one hemisphere (hemineodecortication) in adult cats, the ipsilateral Cd decreased in volume by 18.1% while the total number of neurons

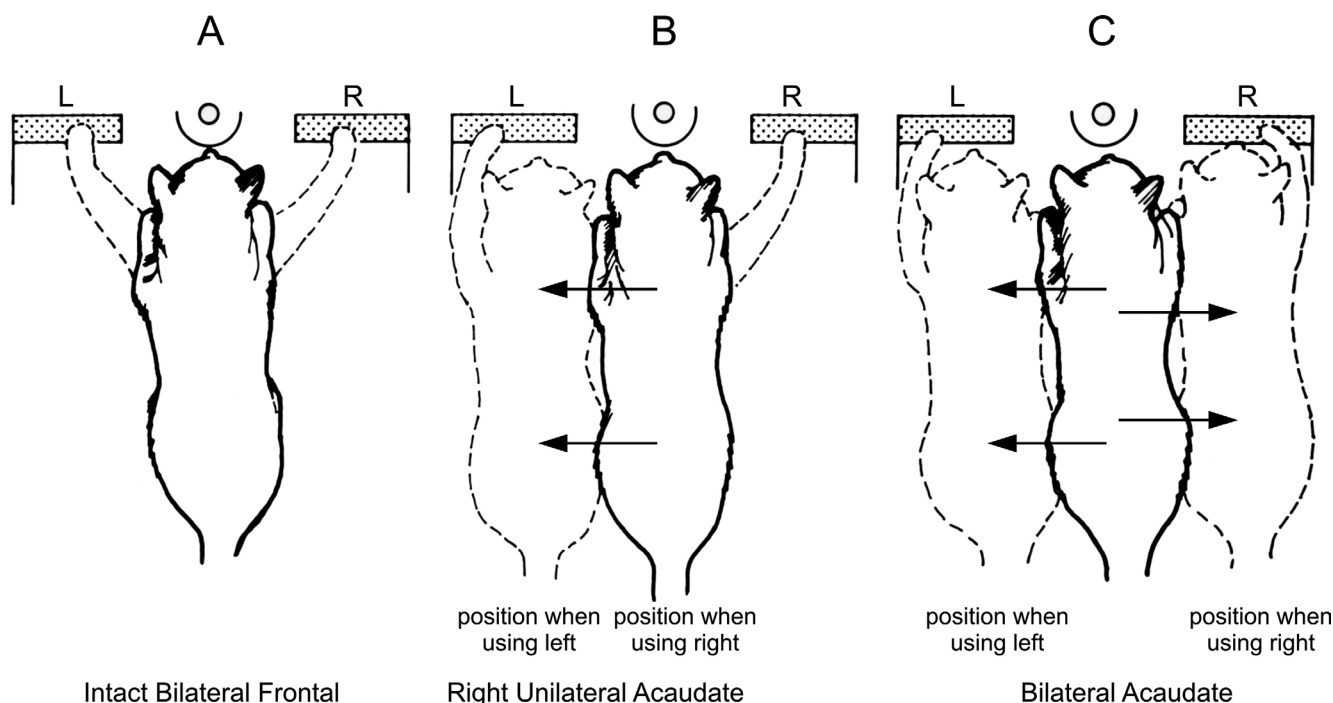


Fig. 3. Schematic representation of the relationship between the cat's body and paw position during the 30×30 and single alternation phases of the bar pressing tasks. The solid lines represent the animal's position while consuming the milk and the dashed lines represent the cat's position while making the paw response. (A) Intact, sham, and afrontal animals; (B) unilateral acaudate, right caudate nucleus removed; (C) bilateral acaudate, note that the postural body shift occurs for both paws. (Reprinted from *Experimental Neurology* Vol. 53, Olmstead CE, Villablanca JR, Marcus RJ, Avery DL, "Effects of caudate nuclei or frontal cortical ablation in cats. IV, Bar pressing, maze learning and performance", p. 670–693, (C) 1976 with permission from Elsevier).

and glial cells decreased correspondingly by 21.8% and 19.9%, respectively (Loopuijt et al. 1997). The caudate hypertrophy is a unique phenomenon which we have not seen in any other experimental setting despite our extensive experience with brain lesions; e.g., the ipsilateral thalamus decreased in size in the very same animals in which the CdN increased in size (Loopuijt and Villablanca 1993). It is tempting to propose that this CdN hypertrophy is an attempt to compensate for the ipsilateral loss of neocortex. It is unfortunate that the Cd hypertrophy was a post-mortem finding such that no additional testing was done; however, we can at least say that no obvious peculiarities were observed in the daily activities of these cats.

We measured the volume of the putamen to screen for any compensatory changes associated with Cd volumetric alterations (Loopuijt and Villablanca 1997). We found no changes after the frontal cortex resection performed prenatally. In addition, the volume of the putamen did not change after hemineodecortication in adulthood. However, a similar resection in neonatal cats resulted in a 27.0% volume increase of the ipsilateral putamen. Therefore, the trend for the neostriatum to compensate for neocortical volume loss still persisted in neonatal cats, but was reflected in putaminal hypertrophy.

The D2 dopamine receptor density increased ipsilaterally (by 101%) and contralaterally (by 77%) in the anterolateral Cd of neonatally as compared to adult hemineodecorticated cats (Loopuijt et al. 1998). There were no significant differences between adult hemineodecorticate and intact cats. At the time of the resection in neonatal cats the density of D2 receptors is still increasing and this may explain the adaptation of receptor density following neodecortication at this age.

The case of a single monkey deserves mentioning. The authors (Denny-Brown and Yanagisawa 1976) performed transcortical aspiration of the Cd bilaterally (although no histological evidence was provided). The animal was observed in its cage, but no systematic tests were applied. The outstanding change was hyperactivity, i.e., pacing the cage back and forth compulsively. Weeks later the pacing changed into circling the cage. Compulsive visual activity (stimulus binding) was also seen. All these activities ceased when the observer could not be seen by the monkey. As with our cats, this animal did not show any gross neurological abnormalities.

SELECTIVE DAMAGE TO THE CAUDATE NUCLEI IN HUMANS

We did not find reports of selective, focal damage to the CdN in humans prior to our review of 1982 (Villablanca and Olmstead 1982); however, a number of papers have been published thereafter. A brief review of the findings follows.

A metanalysis covering reports through 1992 (Kailash and Marsden 1994) identified 20 cases with extensive unilateral damage and only 1 case with selective bilateral damage to the Cd nuclei. By far, most of these patients (86%) did not show neurological abnormalities but, instead, presented with abnormal behavior. Seven patients showed abulia (defined as loss of drive or apathy) and 3 other exhibited disinhibition/hyperkinesia. In addition, the review included 13

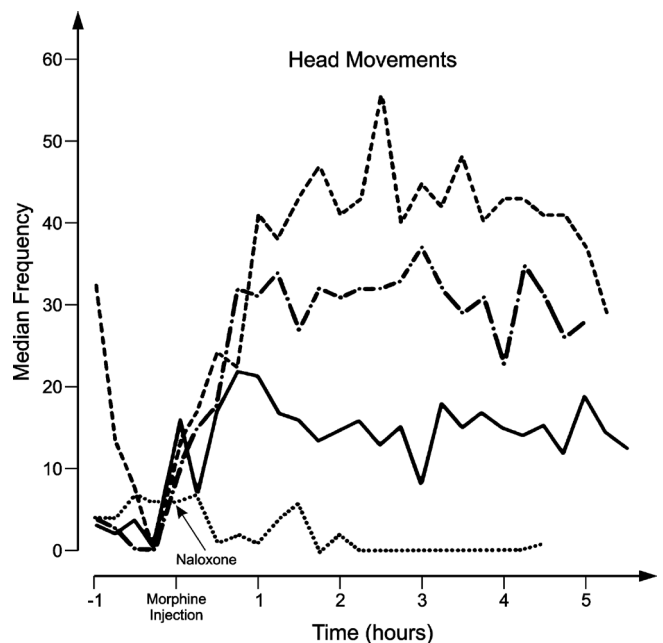


Fig. 4. Shows that the frequency of stereotyped head movement produced by a single injection of morphine in intact cats is markedly reduced in cats with caudate nuclei removal. The values are the median frequency per 2 min video samples taken at 15 min intervals after the injection of morphine (2.0–3.0 mg/kg i.p.) or naloxone (1.0 mg/kg i.p.). Cats with more than 65% caudate tissue removal (___), cats with less than 65% removal (_ _ _), intact cats with a morphine injection (- - -), intact cats with a single naloxone injection (.....). Note that the frequency of the head movements was substantially reduced in the cats with the caudate removed and that this decrease was proportional to the extent of the removal. Reprinted from Villablanca et al. 1982 [with permission from *Acta Neurobiol Exp* (Wars)].

patients with bilateral- and 95 cases with unilateral damage to the Cd plus the putamen. Forty six percent of these patients showed behavioral symptoms only. These consisted mostly of abulia with or without obsessive compulsive behavior/disinhibition. A major conclusion was that lesions of the CdN cause behavioral abnormalities more often than motor disorders. Consequently, the authors commented that “current concepts of basal ganglia organization and function do not fully explain the disorders observed in man when the Cd nuclei are damaged by crude pathology” (Bhatia and Marsden 1994)

Additional and important information can be gleaned from some of the individual papers included in the above metanalysis. In a study of 1 patient with bilat-

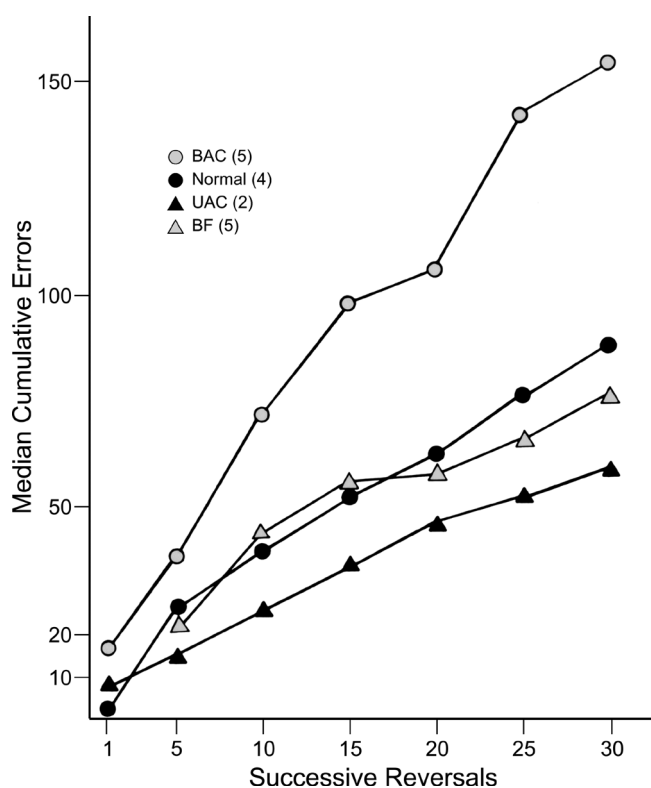


Fig. 5. Median cumulative errors as a function of successive 5×5 spatial reversals in the T-maze task for the 4 groups of cats. (BAC) Bilateral acaudates; (Normal) combined normal and sham operated cats; (UAC) unilateral acaudate cats; (BF) bilateral acaudate animals. Note the substantial increase in the number of errors occurring when the rewarded side of the maze was reversed. (Reprinted from *Experimental Neurology* Vol. 53, Olmstead CE, Villablanca JR, Marcus RJ, Avery DL, “Effects of caudate nuclei or frontal cortical ablation in cats. IV, Bar pressing, maze learning and performance”, p. 670–693, (C) 1976 with permission from Elsevier).

eral- and 11 with unilateral caudate lesions, the authors (Mendez et al. 1989) fully document cognitive deficits using appropriate psychometric tests. The patients were impaired in tasks requiring planning and sequencing. They had short attention spans and decreased recall of episodic and semantic items. Some, depending on the size of the lesions, became impulsive and disinhibited. In another single case of bilateral selective Cd damage, the authors reported a “dramatic personality change manifested by alterations in affect, cognition and self-care” (Richfield et al. 1987) together with hypersexuality. Psychological testing revealed cognitive decline. The above two papers noticed similarities between the symptoms in their patients and the early manifestations of Huntington’s disease.

A well documented case, involving bilateral, selective, infarctions of the Cd nuclei, was reported more recently (Narumoto et al. 2005). The patient showed stimulus-bound behavior, distractibility, and perseverative/obsessive compulsive behavior, all in absence of neurological abnormalities. The authors commented that “The Cd nuclei might be critical for the intentional control of behavior and thought” (Narumoto et al. 2005). Another single case of bilateral CdN ischemia, also almost selective, had been reported previously (Canavero and Fontanella 1998). Aloofness/indifference, lack of concern for daily activities, and compulsive touching of people and objects were reported, together with prospective memory decline and deficits in tasks involving planning.

As described above, there certainly are some basic similarities between the manifestations of extensive Cd damage in humans, which does not need to be bilateral, and the effects of bilateral CdN removal in our cats (and in the one monkey). Most important was that the effects of the removal were expressed in the behavioral/psychological/psychiatric realm, in almost complete absence of neurological perturbations. The salient effects, common to humans and animals, were stimulus binding, obsessive behavior, and perseveration (together with hyperactivity, which, as indicated previously, we see as a non specific change).

OTHER RELEVANT FINDINGS IN HUMANS

The CdN has been implicated in the pathophysiology of a number of conditions including: (1) Schizophrenia – in this disease the Cd-putamen volume has been reported to be either increased or to increase after treat-

ment, or to be smaller in women with schizophrenia personality (Heckers et al. 1991, Jernigan et al. 1991, Beckman and Lauer 1997); (2) Obsessive compulsive disorders – in this condition bilateral volume reduction has been reported (Robinson et al. 1995, Luxenber et al. 1998); although others have described increased CdN volume (Scarone et al. 1992); (3) Tourette syndrome – including bilateral Cd volume reduction (Peterson et al. 1993, Olson 2004); (4) Attention deficit hyperactivity disorders (Castellanos et al. 1994, Canavero and Fontanella 1998); (5) Autism (Haznedar et al. 2006).

In addition, the right anteromedial and the medial CdN were shown to be activated in functional MRI studies of individuals engaged in intense romantic love (Aron et al. 2005). We would concur with this notion; however, we are not suggesting that in absence of the CdN love is impossible.

CONCLUSIONS

Based on the combined information presented above, we propose that the specific role of the Cdn is to control approach-attachment behavior and affect, ranging from plain approach to a target to romantic love. This putative function would account well for the CdN involvement in the pathophysiology of the clinical syndromes listed above, all of which feature a compromised approach-attachment-affect behavior. In addition, the CdN contributes importantly to body and limbs posture as well as to the speed and accuracy of directed movements. This role was not apparent upon observation of spontaneous behavior, but was clearly exposed by appropriate tests (i.e., the bar pressing and paw usage tasks). The human studies do not report this postural role, but this might be due to lack of adequate testing. Other CdN functions appear to be shared with the frontal cortex, albeit in many cases, with distinct contributions from each of these two sites. For example, in the performance tasks (BP and maze learning), the main problems for the cats with frontal cortex removal were unmotivated, slow and irregular behavior, while for the acaudate animals the deficits were different, and included diminished speed and accuracy of directed movements, inability to perform alternations (due to perseveration), as well as the need for the postural adjustment of body and limbs noted above. For other deficits, e.g., the paw contact placing reaction and sleep-waking, the deficits were similar for acaudate and afrontal cats alike. In terms of modulation of sleep-

waking and motor activity levels, we have proposed that the CdN and the frontal cortex are components of a telencephalic inhibitory system that normally balances the powerful posterior ventral-diencephalic and brain stem arousal sites (Villablanca 2004). We believe that this function sharing accounts for the unique Cdn hypertrophy following removal of the frontal cortex in fetal cats. In addition, we showed another unique role for the Cd; this was the exclusive mediation by this n. of the species-specific behavioral effects of a single dose of morphine in cats. It would be highly interesting to test if acaudate cats would also react differently to the repeated administration of morphine (i.e. tolerance, withdrawal effects, and addiction).

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