Aggressive Behavior, Increased Accumbal Dopamine, and Decreased Cortical Serotonin in Rats

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Dopamine (DA) and serotonin have been implicated in the regulation of aggressive behavior, but it has remained challenging to assess the dynamic changes in these neurotransmitters while aggressive behavior is in progress. The objective of this study was to learn about ongoing monoamine activity in corticolimbic areas during aggressive confrontations in rats. Male Long–Evans rats were implanted with a microdialysis probe aimed at the nucleus accumbens (NAC) or medial prefrontal cortex (PFC); next, 10 min samples were collected before, during, and after a 10 min confrontation. Rats continued to display aggressive behavior while being sampled, and they performed two to six attack bites as well as 140 sec of aggressive acts and postures. Dopamine levels in NAC were significantly increased up to 60 min after the confrontation. Peak levels of 140% were achieved ~20–30 min after the confrontation. No concurrent changes in accumbal serotonin levels were seen during or after the confrontation. Dopamine and serotonin levels in PFC changed in the opposite direction, with a sustained decrease in serotonin to 80% of baseline levels during and after the confrontation and an increase in dopamine to 120% after the confrontation. The temporal pattern of monoamine changes, which followed rather than preceded the confrontation, points to a significant role of accumbal and cortical DA and 5-hydroxytryptamine in the consequences as opposed to the triggering of aggressive acts. The increase in accumbal DA in aggressive animals supports the hypothesis that this neural system is linked to the execution of biologically salient and demanding behavior.

Key words: aggression; dopamine; serotonin; nucleus accumbens; prefrontal cortex; rats; microdialysis; behavior

The proposal of a deficit in brain serotonin [5-hydroxytryptamine (5-HT)] as a trait marker for violence-prone individuals is based on measurements that are divorced from the actual behavioral event (Mann et al., 1995; Mann, 1999). In such individuals, low levels of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) were measured in CSF compared with nonviolent controls (Brown et al., 1982; Linnoila et al., 1983; Kruesi et al., 1990; Coccaro, 1992; Virkkunen et al., 1996; Kavoussi et al., 1997). In juvenile monkeys, low levels of 5-HIAA are correlated with increased risk-taking and impulsivity (Higley et al., 1992, 1996; Mehlman et al., 1994). If 5-HT undergoes dynamic state changes (Jacobs and Fornal, 1999) then *in vivo* measures would indicate whether altered serotonin actually is linked to the occurrence of episodes of aggression.

In rodents, aggressive behavior is effectively reduced by treatment with 5-HT_{1A} and 5-HT_{1B} receptor agonists (Olivier and Mos, 1986; Olivier et al., 1987; De Almeida and Lucion, 1997; Miczek et al., 1998; Simon et al., 1998; de Boer et al., 1999; Ferris et al., 1999; Fish et al., 1999). Furthermore, aggression is increased in 5-HT_{1B} receptor knock-out mice (Saudou et al., 1994). 5-HT modulates aggressive behavior in interaction with other neurotransmitters, of which corticolimbic dopamine (DA) continues to be of interest for its critical role in integrating motivation and motor functions (Robbins et al., 1989).

Damage to or pharmacological inhibition of the prefrontal cortex (PFC) can increase aggression, and this effect is hypothesized to be caused by loss of impulse control (Tobin and Logue, 1994). 5-HT receptor binding data from violent suicide victims point to the PFC as a prime area of interest (Pihl et al., 1995; Mann, 1999). Feedback from PFC and innervation from mesencephalic structures establish the nucleus accumbens (NAC) as a critical part of the circuit (Robbins et al., 1989). Dopamine levels in NAC increase during positively reinforced behavior, such as drug-taking (Pettit and Justice, 1991; Weiss et al., 1992; Wise et al., 1995; Ranaldi et al., 1999), food-reinforced behavior (Hernandez and Hoebel, 1988), or sexual behavior (Pfaus et al., 1990; Hull et al., 1993), as well as stressful events such as mild footshock (Abercrombie et al., 1989; Sorg and Kalivas, 1991; Imperato et al., 1992) or social defeat (Tidey and Miczek, 1996). Similar dopamine changes are expected during aggressive behavior because of its stressful, motorically demanding, and even rewarding aspects (to the winner of the confrontation).

In the present experiments, we assessed the dynamic changes in DA and 5-HT in the brains of animals during ongoing aggressive behavior, using *in vivo* microdialysis. The present protocol attempted to differentiate the relative importance of (1) cortical versus accumbal terminals and (2) dopaminergic versus serotonergic activity in a sample of rats with a history of repeated displays of aggressive behavior.

MATERIALS AND METHODS

Subjects. Male Long–Evans rats (Charles River, Wilmington, MA), weighing 350–375 gm at the start, were each housed with a female in a large stainless steel cage (70 × 45 × 45 cm) with sawdust bedding and a clear polycarbonate front panel. The cages were equipped with a wooden structure to provide cover and gnawing material. The female rats' fallopian tubes were ligated under ketamine (100 mg/kg) and xylazine (9 mg/kg) anesthesia to prevent changes in behavior because of the presence of pups. Food and water were available *ad libitum*. The cages were kept in a temperature-controlled (20–21°C) and humidity-controlled (40–50%) vivarium under a reversed light cycle (lights on between 8:00 P.M. and 8:00 A.M.). During the 1 d microdialysis experiment, a divider was lowered to restrict access to the front half of the cage (35 × 45 × 45 cm), which was adapted with a sliding roof with a hole for the microdialysis tubing. All procedures were reviewed and approved by the Tufts University Animal Care and Use Committee, following the principles of the *National Institutes of Health Guide for the Care and Use of Laboratory Animals.*

Resident-intruder confrontations. Three weeks after being housed with a female, the male resident rats confronted a naive male intruder rat (250–300 gm) for 5 min, as described previously (Miczek, 1979). In brief, the female rat was removed from the resident's cage for the duration of the confrontation. The confrontations were terminated 5 min after the first attack bite by the resident, after 20 bites, or after 5 min if no attack occurred. Typically, the resident displays a species-specific pattern of

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Table 1. Aggressive behavior before and during microdialysis testing

Aggression test	*n*	Attack latency	Bite frequency	Aggressive duration
Pretest 1	29	200 (21)	7.7 (1.0)	n.m.
Pretest 2	31	120 (14)	8.3 (1.1)	n.m.
NAC	18	148 (38)	3.1 (0.8)	151 (26)
PFC	15	155 (27)	2.4 (0.5)	106 (18)

Resident males confronted a smaller male intruder in their home cage for 5 min (premicrodialysis tests) or 10 min (microdialysis tests). The frequency of attack bites, latency to the first attack, and total duration of aggressive acts and postures are listed, with latencies and durations given in seconds. Aggressive behavior during microdialysis is presented for the NAC and PFC subgroups. Note that the NAC group contained animals with bilateral implantations, which were sampled on two separate occasions. Data are expressed as averages ± SEM. n.m., Not measured.

aggressive behavior, consisting of pursuits, threats, and attacks. Latency to the first attack and total number of attack bites were monitored. The resident rats showed consistent attack behavior resulting in defeat of the intruder, as defined by the intruder showing a supine posture for at least 5 consecutive seconds and emitting 20–30 kHz ultrasonic vocalizations. This initial intruder confrontation was repeated two times with at least 1 d between tests.

Surgery. Seventeen animals were implanted bilaterally with a CMA/12 guide cannula (CMA Microdialysis, Chelmsford, MA) aimed 2 mm above the NAC. Nineteen animals were implanted unilaterally with a guide cannula aimed 3 mm above the PFC. Coordinates were anteroposterior (AP) +2.0, mediolateral (ML) ±1.5, and dorsoventral (DV) −6.0 from bregma (for NAC) and AP +2.7, ML ±0.7, and DV −2.5 (for PFC), according to Paxinos and Watson (1997). The head-mount was adapted for social interaction tests by adding metal eyelets on either side, allowing for a sturdy connection between the head-mount and the protective wire spring around the microdialysis tubing. After 1 week of recovery, a CMA/12 microdialysis probe (800 μm outer diameter) was lowered into the target area under isoflurane inhalation anesthesia, with a 2 mm exposed membrane in NAC and a 3 mm exposed membrane in PFC. The probe was perfused with artificial CSF (in mM: 147 NaCl, 1.3 $CaCl_2$, 0.9 $MgCl_2$, and 4.0 KCl, pH 6.5–7.0) at a rate of 0.5 μl/min overnight and 1.0 μl/min during the experiment, using a CMA/100 pump. A swivel arm (Med Associates, Georgia, VT), a dual-channel swivel (Instech, Plymouth Meeting, PA), and a 45 cm spring wire protecting the microdialysis tubing (fluorinated ethylene polymer tubing; CMA Microdialysis) allowed free movement of the animal.

Microdialysis protocol. After insertion of the probe, the animal was housed singly overnight for ~16 hr in its modified home cage to allow for neurotransmitters and behavior to reach a stable baseline. On the experimental day, the pump flow was doubled to 1.0 μl/min. After 30 min of stabilization, 10 μl samples were collected every 10 min in a vial containing 5 μl of a stabilizing agent (i.e., 1% ethanol, 0.02% EDTA) using a nonrefrigerated fraction collector (CMA 142). Samples were stored in a −70°C freezer until analysis. Samples were collected for 50 min before a 10 min social confrontation and for 80 min afterward. The social confrontation consisted of the introduction of an experimentally naive intruder rat into the resident's cage, as described above. The intruder was removed after 10 min, corresponding to collection of one sample. Behavior was recorded on videotape during the entire confrontation. In 17 animals with bilateral cannula implantation, a second experiment was performed 1 week after the first experiment to sample the other hemisphere.

HPLC. Samples were analyzed for DA and 5-HT using an LC10-AD pump (Shimadzu, Columbia, MD), a manual injector (model 7125; Rheodyne, Cotati, CA) with a 5 μl sample loop, a microbore column (800 μm × 5 cm) with 3 μm C18 particles (LC Packings, San Francisco, CA), a Decade electrochemical detector (Antec Leyden, Zoeterwoude, The Netherlands), and a data collection and analysis software package (Bioanalytical Systems, West Lafayette, IN). Mobile phase consisting of 25 mM NaH_2PO_4, 50 mM sodium citrate, 27 μM Na_2EDTA, and 2.2 mM 1-octanesulfonic acid, 7% MeOH, pH 4.2, was pumped at a flow rate of 30 μl/min. Retention times for the monoamines were verified daily using a standard solution containing DA, 5-HT, DOPAC, homovanillic acid, and 5-HIAA. Samples were compared using peak heights for DA and 5-HT. Because of their much larger concentration in the samples, the metabolites were not analyzed.

Behavioral analysis. Behavior was recorded on videotape for 5 min at 30 min before the confrontation, for the entire 10 min confrontation, and for 5 min at 60 min after the confrontation. Behavioral responses were analyzed using customized software (Tufts University data acquisition program) (Miczek, 1982). The following nonsocial behavioral elements were recorded: walking, rearing, digging, self-grooming, inactivity, lying, eating, and drinking. The following social and aggressive behavioral elements were recorded: nasal contact, anogenital contact, allogrooming, attack biting, aggressive posture, sideways threat, dragging, and chasing (Miczek, 1979, 1982). Frequency and duration of behavioral acts and postures were analyzed for each animal. The duration of aggressive behavior was calculated by combining the durations for aggressive posture, sideways threat, and chasing.

Data analysis and statistics. Dopamine and serotonin baseline levels in individuals were calculated by averaging the baseline samples collected preceding the aggressive confrontation. Neurotransmitter levels during and after the confrontation were expressed as percent baseline for each individual. A one-way repeated measures ANOVA was performed for each data set, followed by planned paired *t* tests comparing baseline with each time point during and after the confrontation. Because of difficulties with keeping probes in place while animals were fighting, the total number of animals differs for each group (see Results). Three animals that stopped displaying aggressive behavior after surgery were excluded from further analysis, and two animals were excluded on the basis of improper probe placement.

RESULTS

Aggressive behavior

In the first confrontation with an intruder, conducted before the start of the microdialysis experiment, resident rats attacked on 29 of 36 occasions; in the second test, resident rats attacked on 31 of 36 occasions. The average attack bite frequency was 7.7 in the first test and 8.3 in the second test, and average latency to first attack decreased from 200 to 120 sec (Table 1).

On the experimental day, animals were connected to a wire spring and swivel arm to allow free movement during sampling. Under these tethered conditions, the average attack bite frequency decreased to 3.0 with a latency of 150 sec to the first attack and an average duration of aggressive acts and postures of 100–150 sec (Table 1). There were no significant differences in the level of aggression displayed during microdialysis between animals with probes in the NAC or PFC. Aggressive behavior in the tethered residents consisted mostly of threats and bites, followed by pinning down the opponent into a supine posture, assuming the aggressive posture, and some chasing if the opponent tried to escape. The restrictions of the microdialysis connections prevented roll-and-tumble fights. An overview of all aggressive acts and other acts and postures before, during, and after the confrontation is presented in Table 2. All animals were motorically more active during the intruder confrontation, as shown by increased walking, rearing, and grooming, compared with the periods before and after the confrontation. Approximately half the time of the confrontation was spent in interactions with the intruder, in part investigative (i.e., nasal contact, anogenital contact, and allogrooming) and in part aggressive. Approximately 1–2 min were spent in salient aggressive acts, such as aggressive posture and sideways threat.

Microdialysis

NAC septi

Seventeen rats were bilaterally implanted with guide cannulas aimed at the NAC septi. Because of technical problems, data were collected from 21 microdialysis probes. One case was excluded because of improper placement (Fig. 1), and two animals were excluded because of a lack of aggression after surgery. Dopamine levels in NAC significantly increased after the termination of the aggressive encounter (Fig. 2*A*) (one-way repeated measures ANOVA; $F = 3.89$; $p < 0.001$). The increase reached its peak 20–30 min after the confrontation and remained significantly elevated afterward. Serotonin levels in NAC (Fig. 2*A*) were not changed significantly (one-way repeated measures ANOVA; $F = 1.36$; $p = 0.213$).

Table 2. Duration of aggressive and nonaggressive acts and postures during microdialysis

	Nucleus accumbens (n = 18)			Prefrontal cortex (n = 15)		
	Before	Confrontation	After	Before	Confrontation	After
Rearing	14.4 (7.0)	31.2 (5.9)	6.2 (3.9)	0.8 (0.6)	35.3 (7.6)	3.1 (1.6)
Walking	6.3 (2.4)	53.9 (3.9)	6.3 (2.5)	1.2 (1.1)	47.7 (4.4)	5.2 (1.8)
Self-grooming	29.1 (13.0)	55.6 (17.1)	34.5 (14.6)	25.3 (14.1)	43.0 (9.6)	8.4 (3.7)
Digging	3.7 (1.8)	0.6 (0.5)	0.4 (0.2)	0.4 (0.4)	0.6 (0.3)	0.7 (0.6)
Inactive sitting	146.3 (31.4)	130.2 (19.9)	120.0 (29.7)	186.8 (33.9)	235.4 (26.0)	191.4 (26.8)
Lying	68.5 (25.1)	7.1 (7.1)	106.0 (33.4)	53.1 (29.3)	2.5 (1.9)	22.7 (16.9)
Nasal contact	n/a	72.1 (8.4)	n/a	n/a	66.6 (8.2)	n/a
Allogrooming	n/a	28.2 (5.5)	n/a	n/a	24.6 (4.2)	n/a
Anogenital contact	n/a	37.5 (5.1)	n/a	n/a	19.4 (3.4)	n/a
Aggressive posture	n/a	57.8 (18.3)	n/a	n/a	26.9 (7.0)	n/a
Sideways threat	n/a	63.1 (15.7)	n/a	n/a	53.4 (13.7)	n/a
Chasing	n/a	1.4 (0.8)	n/a	n/a	0.4 (0.2)	n/a

Behavior was recorded on video during baseline sampling (Before), during the confrontation, and 1 hr after the confrontation (After), and analyzed afterward using a computerized scoring system. All data are durations in seconds and are expressed as averages ± SEM. For frequency of attacks, see Table 1. n/a, Not applicable.

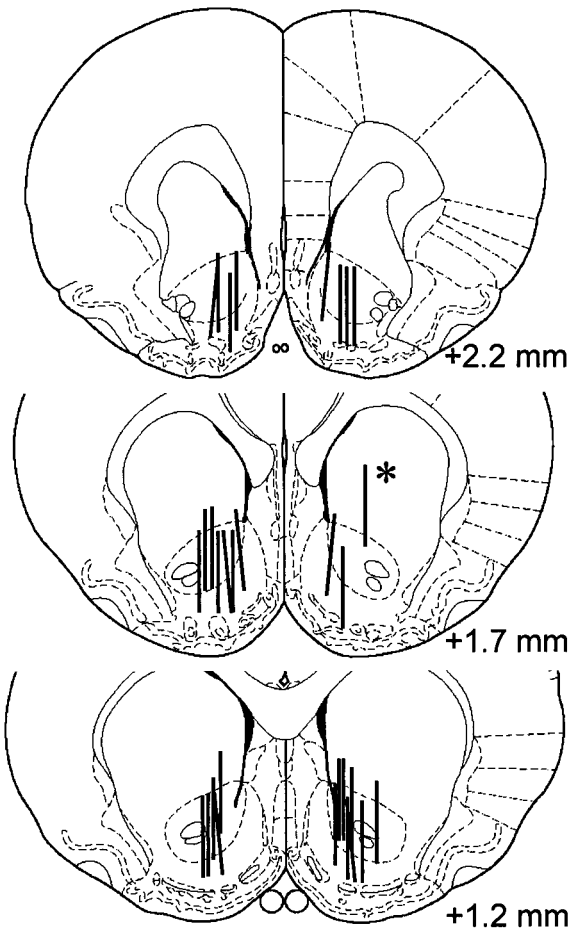

Figure 1. Histological representation of probe placements in NAC. Coronal sections are reproduced from Paxinos and Watson (1997). *Vertical bars* represent the 2 mm exposed membrane of each microdialysis probe. Probes were implanted at random in the left or right hemisphere. *Asterisks* indicate probe placements that were excluded from data analysis.

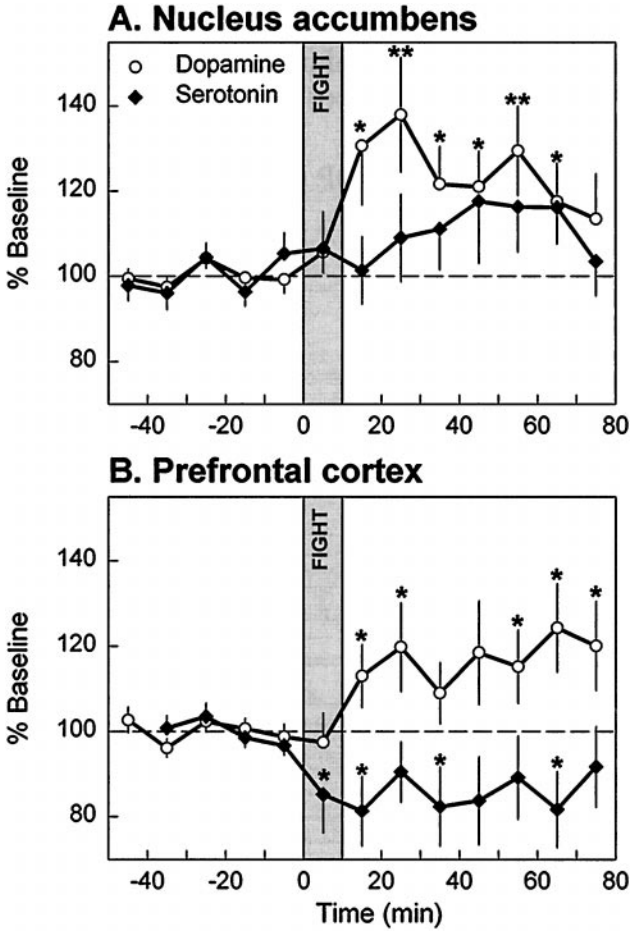

Figure 2. Dopamine and serotonin extracellular concentrations in NAC (*A*; n = 18) or PFC (*B*; n = 15) of male resident rats. Ten minute samples were collected 50 min before, during, and 80 min after a confrontation with a smaller male intruder. The *vertical gray bar* indicates the 10 min period of actual physical confrontation. *Filled diamonds*, Serotonin; *open circles*, dopamine. *Asterisks* indicate a significant change from baseline levels, as assessed by planned paired t tests ($^{*}p < 0.05$; $^{**}p < 0.01$).

PFC

Nineteen rats were implanted with a unilateral guide cannula aimed at the PFC. Data were successfully obtained from 17 microdialysis probes. Their placements were confirmed to be in the medial PFC, except for one case (Fig. 3). One animal was excluded because of a lack of aggression after surgery. Cortical serotonin decreased significantly during and after the confrontation (Fig. 2*B*) (one-way repeated measures ANOVA; $F = 2.070$; $p = 0.050$). Cortical dopamine, in contrast, increased significantly after the confrontation (one-way repeated measures ANOVA; $F = 2.21$; $p = 0.025$). The decline in cortical 5-HT that began during the confrontation persisted for >1 hr after the confrontation.

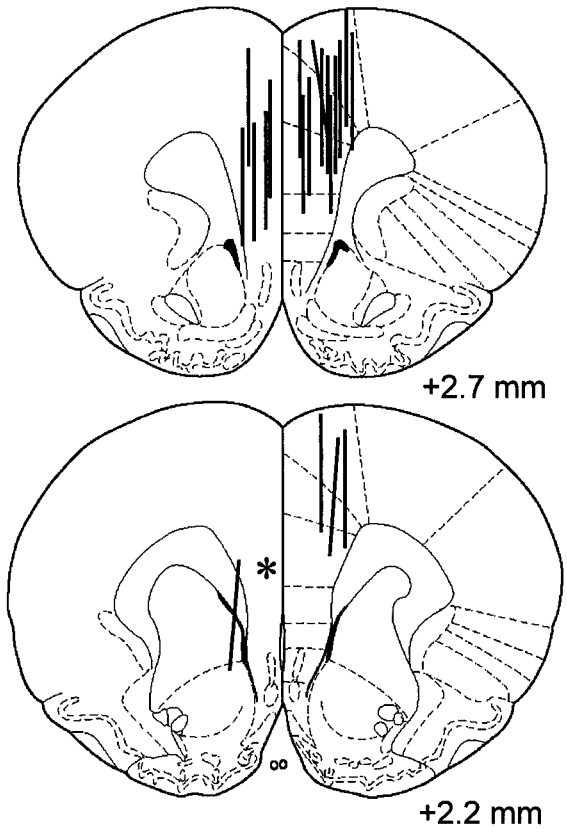

Figure 3. Histological representation of probe placements in PFC. Coronal sections are reproduced from Paxinos and Watson (1997). *Vertical bars* represent the 3 mm exposed membrane of each microdialysis probe. See Figure 1.

DISCUSSION

The current experimental approach enabled the characterization of behavioral and corticolimbic DA and 5-HT activity in association with an aggressive encounter in rats. The data suggest a dissociation between DA and 5-HT activity in NAC and PFC over the course of the aggressive confrontation. First, DA increased in NAC and PFC after the confrontation, whereas accumbal 5-HT remained unaltered. Second, cortical 5-HT decreased during and after the confrontation. Changes in neurotransmitter levels persisted for at least 1 hr after the confrontation.

The dissociation between accumbal and cortical DA and 5-HT activity was also prominent in a parallel study with rats that engaged daily in fighting, at the same time every day for 10 consecutive days. In the absence of the actual fighting behavior on day 11, the aggressive rats showed increased DA immediately preceding the time when they used to start a confrontation with an opponent on previous days, whereas 5-HT decreased thereafter (Ferrari et al., 1998). The dopamine increase is interpreted to reflect behavioral activation in anticipation of the confrontation, and the serotonin decrease may reflect inhibition of aggressive behavior.

The increased DA in NAC and in PFC after aggressive behavior is reminiscent of similar changes in several other significant behavioral contexts. Converging evidence prompts an interpretation of mesocorticolimbic DA as a more integrative system, although the 10–20 min sampling periods for neurotransmitter measurement cannot match the rapid bursts of behavioral acts. For example, increases in accumbal DA have been measured during foraging or the initiation of feeding bouts (Hernandez and Hoebel, 1988; Yoshida et al., 1992; Westerink et al., 1994; Feenstra and Botterblom, 1996) or in the appetitive as well as consummatory phases of copulatory activity (Pfaus et al., 1990; Damsma et al., 1992; Mas et al., 1995; Pfaus et al., 1995; Sato et al., 1995). Importantly, DA changes have been measured after both socially rewarding and aversive events (Mos and van Valkenburg, 1979; Tizabi et al., 1980; Louilot et al., 1986; Haney et al., 1990; Mas et al., 1990). Under the present conditions, dopamine levels increased by 30–40% above baseline after aggressive episodes, and this increase was approximately half of that measured in defensive rats that were threatened by an aggressive opponent (Tidey and Miczek, 1996). The present data highlight an important role for corticolimbic DA as a consequence of aggressive behavior. These data need to be reconciled with the more common interpretation that cortical and accumbal DA may serve a behaviorally integrating function, enabling patterned acts and postures while attending to communicative signals (Le Moal and Simon, 1991). Further support for this hypothesis is derived from the observation that accumbal DA increased in anticipation of a confrontation (Ferrari et al., 1998).

Methodological issues limit the interpretation of rises in DA, particularly the precise anatomical delineation of the cell groups from which dialysis samples originate, and also the sampling interval across which the measured value integrates. It may be possible to detect much larger increases in DA if the measurements could differentiate between core and shell regions of the NAC, as has been demonstrated with studies on feeding behavior (Kelley, 1999), and if they coincided with the behavioral point event more immediately (Wise et al., 1995). The present study could not accomplish such anatomical precision because of the length of the probes. Our sampling intervals did not allow a differentiation between the rise of DA in NAC versus PFC. Such information would contribute to resolving the proposed functional differentiation between these dopaminergic terminal areas (DiChiara, 1997).

The evidence in support of an inhibitory influence of 5-HT on aggressive behavior derives mainly from assays of CSF or tissue that are separated from the behavior in time, pointing to a trait (Mann et al., 1995; Mann, 1999). Indices of low serotonin activity in the brain have been associated with increased levels of aggression and violent behavior, as measured by decreased 5-HT in brain tissue in aggressive mice (Giacalone et al., 1968; Welch and Welch, 1968; Haney et al., 1990) and by decreased levels of 5-HIAA in CSF in violent humans (Brown et al., 1982; Linnoila et al., 1983; Kruesi et al., 1990; Coccaro, 1992; Virkkunen et al., 1996; Kavoussi et al., 1997) and aggressive macaques (Higley et al., 1992, 1996; Mehlman et al., 1994). Selective serotonergic agonists at the 5-HT_{1A} and 5-HT_{1B} receptor subtypes, as well as serotonin reuptake inhibitors, have been proven very effective in reducing aggressive behavior in rodents and humans (Olivier and Mos, 1986; Olivier et al., 1987; Miczek et al., 1998; de Boer et al., 1999; Ferris et al., 1999; Fish et al., 1999). However, CSF measurements and systemic pharmacological manipulations are removed from the critical neural sites of action. Moreover, these changes are seen in individuals that are at steady-state conditions, long after aggressive acts have taken place, more likely reflecting an aggressive trait rather than the neural dynamics of an aggressive act. The present study showed that acute changes in serotonin levels do occur during and after an aggressive confrontation. It remains challenging to closely match the neurotransmitter sampling scheme to the fast-changing behavioral acts during an aggressive confrontation. Whether these changes occur because of initiation or termination of aggression or because of a general change in behavioral state cannot be determined with the present temporal resolution. The fact that the changes lasted up to 1 hr afterward may rather reflect a change in behavioral state that outlasted the actual execution of the behavior.

The functional significance of corticolimbic serotonin extends from sleep, perceptual processes, and motor control to many appetitive behaviors, including aggressive behavior (Lucki, 1998). The steady basal serotonergic activity recorded in dorsal raphe neurons in cats has been shown to be decreased during sleep and increased with arousal (Jacobs and Fornal, 1999). Supporting data were obtained from microdialysis studies, which showed that various stressful and nonstressful conditions caused a similar increase in extracellular 5-HT in several forebrain sites (Petty et al., 1994;

Rueter and Jacobs, 1996; Wilkinson et al., 1996). However, the role of 5-HT in stress responses appears to be anatomically differentiated and is not limited to increases. For example, forced swimming caused 5-HT increases in striatum and decreases in amygdala and lateral septum in rats, whereas 5-HT levels in hippocampus and frontal cortex remained unchanged (Kirby et al., 1997). Also, withdrawal after prolonged self-administration of cocaine (a profoundly stressful experience) caused a drop in accumbal serotonin levels (Parsons et al., 1995). Moreover, there is evidence for stressor-specific changes in the frontal cortex, with increased 5-HT after saline injection and decreased 5-HT after forced swimming (Adell et al., 1997). It becomes apparent that precise timing and direction of changes in major terminal areas for serotonin projections depend on the type of stress experience and the relationship to various complex motor and cognitive behaviors. Our finding that serotonin was decreased in PFC but not NAC after aggression adds evidence to this more complex pattern but fails to help resolve the puzzle of stress- and location-dependent changes in serotonin levels. Recent data collected in rats that confronted an opponent for 10 consecutive days at the same time every day show decreased accumbal serotonin on the day after the last confrontation at the time when the confrontation would have taken place previously (Ferrari et al., 1998). These data indicate that serotonin decreases may be associated with anticipation and possibly inhibition rather than direct execution of aggressive behavior. Whether similar 5-HT decreases would occur in PFC needs to be investigated further.

Because individuals that are more prone to aggression may be characterized by a serotonin deficiency, we were interested in determining whether rats that were highly aggressive versus those that were nonaggressive would show differential responses in dopamine or serotonin changes during aggression. Using the present conditions and stock of animals, however, a moderate level of aggression was displayed, and too few animals were highly aggressive (e.g., >10 attack bites per 5 min) to allow such a comparison to be made. In addition, marked individual variations in amine changes was observed, which may have occurred in part because of differences in precise anatomical location. Therefore, at present, it remains unclear whether there might have been a correlation between the number of aggressive acts or the duration of aggressive behavior and the magnitude of change in accumbal DA or 5-HT levels. Future studies could address this issue more directly by studying selectively bred rat or mouse lines that show high versus low levels of aggressive behavior (Lewis et al., 1994).

In conclusion, our data support a role for dopamine and serotonin in the consequences of aggressive acts that appear important for the future occurrence of this behavior. Whether these acute changes are correlated with long-term changes in individuals that are more prone to violent episodes remains to be determined. A future task would be to explore strains of high- and low-aggressive animals and to explore both state (i.e., acute 5-HT changes) and trait (i.e., baseline 5-HT and 5-HIAA levels) differences between them.

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