ELSEVIER

Psychiatry Research 104 (2001) 27–37

PSYCHIATRY RESEARCH

www.elsevier.com/locate/psychres

Serotonin, testosterone and alcohol in the etiology of domestic violence

David T. George[a,*], John C. Umhau[a], Monte J. Phillips[a], Devadatham Emmela[a], Paul W. Ragan[b], Susan E. Shoaf[a], Robert R. Rawlings[a]

[a] *Laboratory of Clinical Studies, DICBR, National Institute on Alcohol Abuse and Alcoholism, 10 Center Drive, Bethesda, MD 20892, USA*

[b] *Department of Psychiatry, Vanderbilt University Medical Center, 1211 22nd Ave. S., Nashville, TN 37232, USA*

Received 19 December 2000; received in revised form 22 June 2001; accepted 5 August 2001

Abstract

In a previous study we administered the panicogenic agent sodium lactate to a select group of perpetrators of domestic violence and comparison groups. Results of that study showed that perpetrators exhibited exaggerated lactate-induced fear, panic and rage. In this current study, we compared the cerebral spinal fluid (CSF) concentrations of 5-hydroxyindoleacetic acid (5-HIAA) and testosterone obtained from perpetrators of domestic violence and a group of healthy comparison subjects. All subjects were assessed for DSM-III-R diagnoses. Perpetrators with alcohol dependence (DV-ALC) ($n = 13$), perpetrators without alcohol dependence (DV-NALC) ($n = 10$) and healthy comparison subjects (HCS) ($n = 20$) were clinically assessed using the Spielberger Trait Anxiety, Brown–Goodwin Aggression Scale, Buss Durkee Hostility Inventory and Straus Conflict Tactics. Following an overnight fast and bed rest, subjects received a lumbar puncture to obtain CSF concentrations of 5-HIAA and testosterone. Perpetrators scored significantly higher on measures of aggression than HCS. DV-NALC had significantly lower concentrations of CSF 5-HIAA and higher Straus Conflict Tactics (CT) physical violence scores than DV-ALC and HCS. DV-ALC had significantly higher concentrations of CSF testosterone than DV-NALC. DV-ALC also had significantly higher Straus CT physical violence scores than HCS. DV-NALC and DV-ALC differed on 5-HIAA concentrations, testosterone concentrations, Straus CT physical violence scores and alcohol dependence. These results suggest that DV-NALC and DV-ALC groups could have different biological mechanisms mediating domestic violence.

Keywords: Aggression; Alcoholism; Rage; Cerebral spinal fluid (CSF); Fear conditioning

* Corresponding author. Tel.: +1-301-496-9705; fax: +1-301-402-1543.
E-mail address: tedg@niaaa.nih.gov (D.T. George).

0165-1781/01/$ - see front matter
PII: S0165-1781(01)00292-X

1. Introduction

Two nationally conducted surveys in 1975 and 1985, involving a representative sample of approximately 6663 American families, found that 16% of the men and women had been physically assaulted by their spouse or significant other in the year prior to the survey (Straus and Gelles, 1986). Fifty percent of the perpetrators were either binge drinkers or consumed 3–5 drinks of alcohol per day. Perpetrators with the highest chronic alcohol consumption were the most likely to be violent (Kantor and Straus, 1990).

In a previous study investigating the link between fear and aggression in perpetrators of domestic violence, we administered the panicogenic agent sodium lactate to a select group of perpetrators and comparison groups (George et al., 2000). Results of the study showed that perpetrators exhibited exaggerated lactate-induced fear, panic and rage; some perpetrators reported that they experienced similar symptoms at the time of domestic violence. Perpetrators also showed a preponderance of DSM-III-R diagnoses of anxiety/phobic disorders. These results led us to examine the biological mechanisms, which could contribute to these exaggerated fear-related responses and ultimately to domestic violence.

One possibility is that perpetrators could have a disturbance in serotonin (5-HT) metabolism. Both human (Virkkunen et al., 1987, 1989a,b, 1994a; Roy et al., 1988; Limson et al., 1991) and animal studies (Higley et al., 1992; Mehlman et al., 1994; Doudet et al., 1995) have shown an inverse relationship between the cerebrospinal fluid (CSF) metabolite of 5-HT, 5-hydroxyindolacetic acid (5-HIAA), and aggression. Administration of pharmacological agents that reduce central 5-HT concentrations, either by depleting tryptophan (Chamberlain et al., 1987; Cleare and Bond, 1995; Moeller et al., 1996) or by blocking 5-HT synthesis (Katz and Thomas, 1976; Valzelli et al., 1981), typically cause an increase in aggression. Conversely, administration of agents that increase 5-HT, either by facilitating its release (Cherek and Lane, 1999) or by blocking its re-uptake (Fava et al., 1991; Salzman et al., 1995; Coccaro and Kavoussi, 1997), generally cause a decrease in aggression.

Studies in humans and animals show that 5-HT modulates (Morrison and Foote, 1986) the structures and neuropathways that mediate fear-related behaviors (Shaikh et al., 1987; LeDoux et al., 1990; Shaikh and Siegel, 1994; Morgan and LeDoux, 1995; Armony and LeDoux, 1997; Davis, 1997, 1998; LaBar et al., 1998; LeDoux, 1998; Hashimoto et al., 1999; Siegel et al., 1999). For example, 5-HT modulates the startle reflex (Davis et al., 1980) as well as sensory input to the thalamus (Marks et al., 1987) and striatum (Reisine et al., 1982) which serves to warn animals of environmental dangers. Serotonin in the medial prefrontal cortex modulates freezing behavior associated with a conditioned fear stimulus (Inoue et al., 1996; Hashimoto et al., 1999). Serotonergic input to amygdala, the medial hypothalamus and the periaquaductal grey (PAG) is involved with the control as well as the expression of fear-associated 'fight' or 'flight' behaviors (Spoont, 1992; Shaikh et al., 1997; Viana et al., 1997; Stutzman et al., 1998).

Another possible biological mechanism is that perpetrators could have a disturbance in testosterone metabolism. Evidence for testosterone's possible role in modulating fear-related responses and aggression is derived from both animal and human studies. For example, animal studies show that testosterone-dependent aggression occurs in non-human mammals (Albert et al., 1993; Higley et al., 1996). Evidence for testosterone's role in human physical aggression comes from studies showing that some subgroups of violent subjects have higher plasma (Ehrenkranz et al., 1974; Mattsson et al., 1980), saliva (Soler et al., 2000) and CSF testosterone (Virkkunen et al., 1994b) concentrations than non-violent controls. Also, it has been shown that adolescent males with high plasma testosterone concentrations are more irritable and more likely to respond aggressively to provocation and threats than subjects with lower testosterone concentrations (Olweus et al., 1980, 1988). Finally, subjects receiving testosterone are more likely to have an aggressive response to perceived threats than subjects receiving placebo (Pope and Katz, 1990; Su et al., 1993; Pope et al., 2000).

How testosterone could facilitate these fear-related responses and aggression is not known.

One possibility is that testosterone modulates 5-HT_{1A} and 5-HT_{2A} receptor activity, which has been shown in animals to directly affect aggression as well as anxiety (Bonson and Winter, 1992; Fink et al., 1999; Zhang et al., 1999). Evidence, pertaining to fear-related responses, is based upon the fact that androgen receptors are present in the same brain regions (i.e. thalamus, frontal cortex, amygdala, hypothalamus, etc.) involved with the control and/or expression of fear-related responses (Clancy et al., 1994; Greco et al., 1996; Finley and Kritzer, 1999; Murphy et al., 1999).

Since a large proportion of perpetrators of domestic violence abuse alcohol, it is necessary to consider what effect alcohol abuse could have on testosterone and 5-HT concentrations. In chronic alcoholics plasma testosterone concentrations may be suppressed by ethanol (Ruusa et al., 1997) but increase during abstinence. In a study of alcoholics starting a treatment program, Irwin et al. (1988) found that 17% had depressed levels of testosterone, which increased to normal levels during abstinence. For alcoholics with normal levels of testosterone, there was no significant increase in testosterone during abstinence. Serotonin metabolism can also be affected by alcohol. Animal studies show alcohol administration causes the release of 5-HT in the brain (Griffiths et al., 1974; Kaneyuki et al., 1991). In chronic alcoholics, CSF 5-HIAA concentrations can be elevated during withdrawal but decline during abstinence (Ballenger et al., 1979; Borg et al., 1985).

There are no animal models for domestic violence, but there are several animal models for aggression (Albert et al., 1993). Albert et al. (1993) discuss both anatomical as well as behavioral evidence showing similarities between defensive aggression in animals and aggression displayed by humans. Defensive aggression occurs in response to an actual or a perceived threat. Exaggerated defensive aggression can result from lesions in several brain regions (e.g. septum, medial hypothalamus). Animals with these lesions are described as hyperirritable or hyperreactive (Albert and Walsh, 1982). Similarly, in various human brain structures pathological lesions increase aggression (Zeman and King, 1958; Reeves and Plum, 1969; Tonkonogy and Geller, 1992). These structures correspond to the same brain regions which control defensive aggression in animals (Shaikh et al., 1985, 1987; Siegel et al., 1999).

In this present study, we compared the CSF 5-HIAA and CSF testosterone concentrations in perpetrators of domestic violence and healthy comparison subjects. To control for the potential effects of chronic alcohol consumption on domestic violence perpetrators, we required that the perpetrators be subdivided into separate groups based on the DSM-III-R diagnosis of alcohol dependence. Perpetrators with alcohol dependence (DV-ALC) had to be abstinent from alcohol for at least 3 weeks prior to the study.

2. Methods

2.1. Subjects

The majority of the perpetrators were recruited through newspaper advertisements entitled, 'Do You Ever Lose Control?' Healthy comparison subjects were recruited from the community, the clinical program of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institutes of Health (NIH) volunteer office. Participants underwent extensive clinical and physical examinations to ensure that they were in good health. Subjects with a history of seizures, head trauma (defined as a period of unconsciousness exceeding 1 h), or medical conditions requiring chronic medications were excluded from participation. Subjects were required to refrain from taking all medications for 3 weeks prior to the study. All subjects had a negative urine drug screen for illicit drugs. Prior to being studied, subjects with a history of alcohol and/or drug abuse were abstinent for >25 days while other subjects abstained from alcohol for at least 72 h. Abstinence was verified by careful questioning of the subject and interviews with spouse or significant other, when available. Pertinent laboratory tests (i.e. liver enzymes, breath alcohol levels) were also obtained prior to the lumbar

puncture (LP) to monitor patient compliance. Subjects who could not remain abstinent (8 of the 13 DV-ALC) were admitted to our inpatient ward and monitored for 3 weeks prior to the LP. Non-alcoholic subjects were permitted small quantities of alcohol up to 72 h prior to the LP.

Following the abstinence period, perpetrators had an electroencephalogram and MRI of the brain to rule-out central nervous system pathology which could contribute to violent behavior. DSM-III-R psychiatric diagnoses were derived using the Structured Clinical Interview (SCID) (Spitzer et al., 1992), which was administered by a social worker with extensive training in interviewing. Subjects with a DSM-III-R diagnosis of either bipolar illness or schizophrenia were excluded.

Subjects were classified into three groups. The first group consisted of 13 male perpetrators of domestic violence who fulfilled DSM-III-R criteria for alcohol dependence (DV-ALC); the perpetrators of domestic violence without a diagnosis of alcohol dependence group (DV-NALC) consisted of 10 male subjects. The healthy comparison subjects (HCS) consisted of 20 male subjects who had no history of alcohol abuse, alcohol dependence, or interpersonal aggression and did not fulfill criteria for any DSM-III-R Axis I diagnosis.

The DV-ALC had 11 subjects with anxiety/phobic Axis I disorders. Eleven DV-ALC had antisocial personality/borderline Axis II disorders. The DV-NALC had eight subjects with anxiety/phobic Axis I disorders and one subject with intermittent explosive disorder. DV-NALC also had one antisocial personality disorder and four borderline personality Axis II disordered subjects.

The perpetrator groups consisted of men from a broad range of socio–economic backgrounds ranging from executives to unemployed individuals. Only those subjects who had a history of inflicting repeated acts of significant physical violence (e.g. hitting/punching, aggressive pushing/shoving, choking, using a weapon) toward a significant other were included. At least some of the acts of domestic violence occurred when the perpetrators were not under the influence of alcohol.

Subjects were assessed for age, socio–economic status (Hollingshead Four-Factor Index of Social Position) (Hollingshead and Redlich, 1958), anxiety (Spielberger State and Trait Anxiety Inventory) (Spielberger et al., 1970) and aggression (Brown-Goodwin Lifetime Aggression Scale, Brown et al., 1979; Buss-Durkee Hostility Inventory, Buss and Durkee, 1957). (Some subjects left the research unit before completing all demographic measures.) We also administered the Straus Conflict Tactics (CT) instrument (Straus, 1979, 1990), consisting of 19 questions rating the frequency of specific behaviors (e.g. insulting, kicking and hitting their significant other, etc.) on a scale of 0 (never) to 6 (everyday). Specific subscores were derived from the Straus CT for reasoning (e.g. rational discussion to resolve conflict), verbal aggression and physical violence.

The study was approved by the National Institute on Alcohol Abuse and Alcoholism Institutional Review Board. After a complete description of the study to the subjects, written informed consent was obtained. Twenty of the perpetrators and thirteen of the HCS also participated in the sodium lactate study (George et al., 2000). The sodium lactate study and LP were performed on separate days.

2.2. Cerebrospinal fluid collection and assay procedures

Ten hours prior to the LP all subjects were on overnight bedrest and received nothing by mouth (NPO). The LPs were performed between 09:00 and 10:00. Subjects were in the left lateral decubitus position. The first 12 ml of CSF were collected in a single aliquot, thoroughly mixed, immediately placed on wet ice and quickly stored in aliquots at −80°C. 5-HIAA was quantified by gas chromatography–mass spectrometry using deuterated internal standards (Polinsky et al., 1988) and reported in pmol/ml. CSF testosterone levels were obtained by using a radioimmunoassay procedure (Rahe et al., 1990) and reported in ng/dl.

2.3. Statistical analysis

Group comparisons were performed with anal-

yses of variance. Pairwise comparisons were performed for variables for which ANOVAs were significant. The level of significance was chosen to be $P = 0.05$ for the two variables of primary interest, CSF concentrations of 5-HIAA and testosterone, while $P = 0.01$ was chosen for the 13 subject characterization variables in Table 1. For each statistical test, the adequacy was determined by examining normal probability plots of model residuals, tests of homogeneity of variance and tests of equality of covariate slopes. All of the statistical analyses in this study were performed using the STATISTICA software package (Statsoft, 1994, 1999).

3. Results

There were no significant differences between

Table 1
Subject characteristics (mean ± standard deviation)

	HCS	DV-ALC	DV-NALC	ANOVA, P
Age (years)	39.8 ± 9.1 $n = 20$	34.7 ± 6.4 $n = 13$	39.3 ± 7.7 $n = 10$	$F(2,40) = 1.7$, $P = 0.196$
Weight (kg)	80.9 ± 10.0 $n = 20$	80.1 ± 14.6 $n = 13$	85.3 ± 13.3 $n = 9$	$F(2,39) = 0.6$, $P = 0.580$
Height (cm)	176.8 ± 8.2 $n = 20$	176.1 ± 7.5 $n = 13$	179.3 ± 8.0 $n = 9$	$F(2,39) = 0.5$, $P = 0.625$
Hollingshead Social Position Index	4.2 ± 1.0 $n = 20$	3.4 ± 0.9 $n = 13$	4.1 ± 1.5 $n = 10$	$F(2,40) = 2.4$, $P = 0.106$
Spielberg Trait Anxiety* (a,b)	28.5 ± 8.3 $n = 16$	44.2 ± 7.4 $n = 11$	41.9 ± 13.1 $n = 10$	$F(2,34) = 10.7$, $P < 0.001$
MAST* (a,c)	1.0 ± 1.5 $n = 20$	43.3 ± 15.9 $n = 13$	3.6 ± 4.6 $n = 10$	$F(2,40) = 95.6$, $P < 0.001$
Run-ins with police* (a,b)	0.1 ± 0.3 $n = 18$	8.8 ± 10.7 $n = 13$	2.0 ± 2.0 $n = 10$	$F(2,38) = 7.9$, $P = 0.001$
Number of arrests* (a)	0.1 ± 0.3 $n = 18$	5.6 ± 5.9 $n = 13$	1.0 ± 1.6 $n = 10$	$F(2,38) = 10.4$, $P < 0.001$
Brown–Goodwin Aggression Scale* (a,b)	5.3 ± 4.1 $n = 19$	24.0 ± 8.7 $n = 12$	14.3 ± 6.5 $n = 9$	$F(2,37) = 32.5$, $P < 0.001$
Buss-Durkee Hostility Inventory* (a,b)	15.9 ± 8.5 $n = 16$	48.2 ± 15.3 $n = 12$	43.7 ± 9.9 $n = 9$	$F(2,34) = 32.5$, $P < 0.001$
Straus Conflict Tactics				
Verbal reasoning score	66.7 ± 35.1 $n = 16$	50.0 ± 22.3 $n = 12$	53.1 ± 21.7 $n = 9$	$F(2,34) = 1.3$, $P = 0.275$
Verbal aggression score* (a,b)	4.5 ± 5.8 $n = 16$	45.6 ± 23.0 $n = 12$	39.7 ± 12.7 $n = 10$	$F(2,35) = 31.2$, $P < 0.001$
Violence score* (a,c,b)	0.1 ± 0.4 $n = 17$	4.9 ± 2.4 $n = 9$	12.6 ± 5.1 $n = 9$	$F(2,32) = 57.2$, $P < 0.001$

* Significant group effect at $P < 0.01$. Pairwise comparison significant at $P < 0.01$: a = HCS vs. DV-ALC; b = HCS vs. DV-NALC; c = DV-ALC vs. DV-NALC.

the groups for age, weight, height, or socio–economic status. As expected, MAST scores were higher in DV-ALC due to the diagnosis of alcohol dependence as a criterion for inclusion in this group. Both perpetrator groups had significantly higher Spielberger Trait Anxiety scores than HCS. DV-ALC and DV-NALC scored significantly higher than HCS on measures related to aggression (e.g. Brown-Goodwin, Buss-Durkee Hostility Inventory, Straus CT verbal aggression and physical violence subscores). DV-NALC also scored significantly higher than the DV-ALC on the Straus CT physical violence subscale. DV-ALC and DV-NALC had more run-ins with police than HCS, and DV-ALC had significantly more arrests than DV-NALC and HCS (Table 1).

There was a significant ANOVA for 5-HIAA ($F_{(2,40)} = 3.5$, $P = 0.041$). Pairwise comparisons were then performed (HCS vs. DV-NALC: $F_{(1,40)} = 4.4$, $P = 0.042$; HCS vs. DV-ALC: $F_{(1,40)} = 0.5$, $P = 0.477$; DV-ALC vs. DV-NALC: $F_{(1,40)} = 6.5$, $P = 0.015$) (Fig. 1). DV-NALC [65.9 ± 18.2 (S.D.)] were significantly lower in 5-HIAA than DV-ALC (100.2 ± 37.7) or HCS (92.0 ± 33.5). DV-ALC and HCS were not significantly different.

There was a significant ANOVA for testosterone ($F_{(2,40)} = 7.9$, $P = 0.001$). Pairwise comparisons were then performed (HCS vs. DV-NALC $F_{(1,40)} = 0.05$, $P = 0.824$; HCS vs. DV-ALC $F_{(1,40)} = 13.1$, $P = 0.001$; DV-ALC vs. DV-NALC $F_{(1,40)} = 10.7$, $P = 0.002$) (Fig. 2). DV-ALC (0.25 ± 0.05) were significantly higher in testosterone concentrations than DV-NALC (0.19 ± 0.04) or HCS (0.19 ± 0.05). DV-NALC and HCS were not significantly different.

In order to examine the contribution of anxiety to the above results, we repeated the analyses with Spielberger Trait Anxiety scores as a covariate. The test of the covariate regression coefficient is not significant for testosterone ($\beta = -0.16$, $t_{(33)} = -0.91$, $P = 0.37$) or for 5-HIAA ($\beta = 0.19$, $t_{(33)} = 1.13$, $P = 0.27$). Therefore, the initial results are unlikely to be due to anxiety. Within the DV-ALC and DV-NALC groups, we examined the relationship of testosterone and 5-HIAA with the Brown–Goodwin Aggression Scale, Buss-Durkee Hostility Inventory and Straus CT physical violence subscales. None of the correlations were significant at the $P = 0.05$ level.

4. Discussion

We performed lumbar punctures in healthy

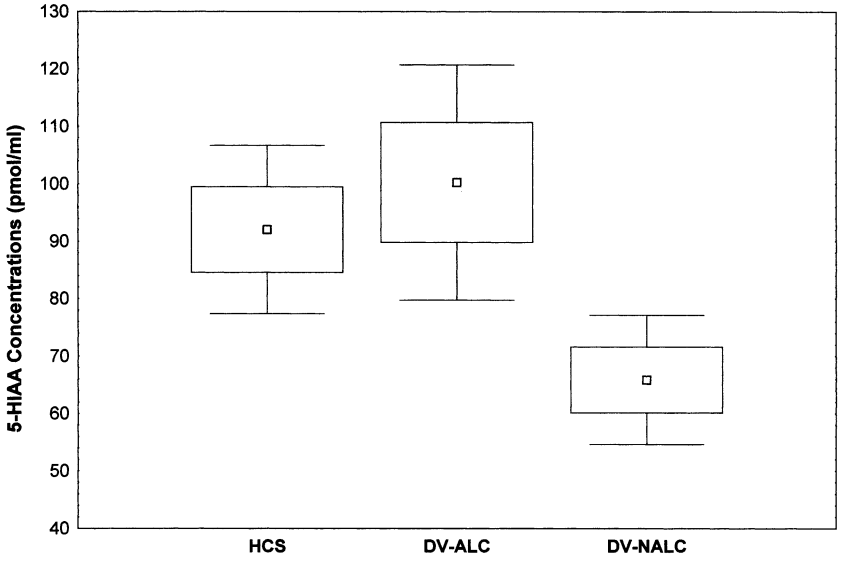

Fig. 1. A comparison of 5-HIAA concentrations. (ANOVA: $F_{(2,40)} = 3.5$, $P = 0.041$. Pairwise comparisons: HCS vs. DV-NALC, $F_{(1,40)} = 4.4$, $P = 0.042$; HCS vs. DV-ALC, $F_{(1,40)} = 0.5$, $P = 0.477$; DV-ALC vs. DV-NALC, $F_{(1,40)} = 6.5$, $P = 0.015$.)

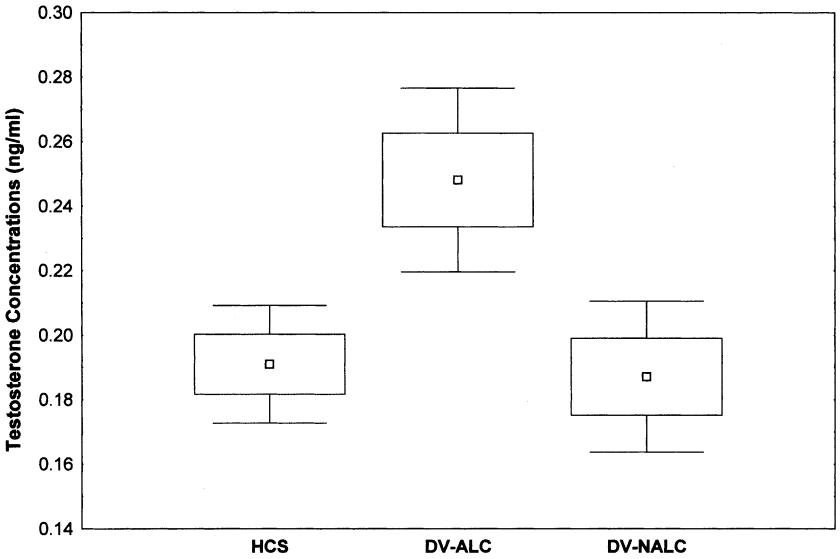

Fig. 2. A comparison of tesosterone concentrations. (ANOVA: $F_{(2,40)} = 7.9$, $P = 0.001$. Pairwise comparisons: HCS vs. DV-NALC, $F_{(1,40)} = 0.05$, $P = 0.824$; HCS vs. DV-ALC, $F_{(1,40)} = 13.1$, $P = 0.001$; DV-ALC vs. DV-NALC, $F_{(1,40)} = 10.7$, $P = 0.002$).

control subjects and a select group of perpetrators of domestic violence, with and without a diagnosis of alcoholism, who had been shown in a previous study to have an exaggerated fear/rage response to the panicogenic agent sodium lactate. In this study we performed group comparisons of CSF 5-HIAA concentrations, CSF testosterone concentrations and measures of aggression. Our present results show that both DV-NALC and DV-ALC group had significantly higher measures of aggression than HCS. DV-NALC had significantly higher Straus CT physical violence scores than DV-ALC. However, only the DV-NALC group had significantly lower concentrations of CSF 5-HIAA and only the DV-ALC group had significantly higher CSF testosterone concentrations.

The DV-ALC group had similar CSF 5-HIAA concentrations to those found in HCS. This result is consistent with the study by Lidberg et al. (1985), who reported that patients convicted of homicide with alcoholism had CSF 5-HIAA concentrations similar to those in HCS. Also, similar results were obtained in the intermittent explosive disordered subgroup of the violent alcoholics in Virkkunen et al. (1994b). The higher testosterone concentration in the DV-ALC group, relative to those found in HCS, is consistent with similar findings in the antisocial personality disordered violent alcoholics studied by Virkkunen et al. (1994b).

The DV-NALC group had similar CSF testosterone concentrations to those found in HCS. There are no CSF testosterone studies on non-alcoholics with which we can compare our result. Our finding of lower CSF 5-HIAA concentrations in the DV-NALC group, relative to the DV-ALC group, is consistent with Lidberg et al. (1985), showing that violent men without alcoholism had lower 5-HIAA concentrations compared with violent men with alcoholism.

As discussed earlier, abstinence in alcoholics can increase testosterone concentrations to *normal* levels. However, the DV-ALC group had significantly higher concentrations than the HCS. Therefore, alcohol withdrawal is an unlikely explanation for the significantly higher testosterone concentrations relative to HCS. Also, as discussed earlier, 5-HIAA levels in alcoholics decrease during abstinence. Ballenger et al. (1979) showed

that alcoholics after 1 month of abstinence had subnormal concentrations of 5-HIAA. Therefore, alcohol abstinence again is an unlikely explanation for the equal concentrations of 5-HIAA in the DV-ALC and the HCS groups since the DV-ALC subjects have been abstinent for approximately a month.

In this article, we explored the role of 5-HT and testosterone in perpetrators of domestic violence who have been previously studied and shown to have fear-induced aggression. We have shown or discussed the following: (1) the HCS and DV-NALC groups differ on 5-HIAA concentrations and Straus CT physical violence scores; (2) the HCS and DV-ALC groups differ on testosterone concentrations, alcohol dependence and Straus CT physical violence scores; (3) the DV-NALC and DV-ALC groups differ on 5-HIAA concentrations, testosterone concentrations, Straus CT physical violence scores and alcohol dependence; (4) alcohol abstinence is not a likely explanation for the DV-NALC and DV-ALC groups' differences in 5-HIAA and testosterone concentrations; (5) 5-HIAA and testosterone concentrations can influence fear-related responses; (6) 5-HIAA and testosterone concentrations are related to aggression; and (7) fear-related responses and aggression are present during acts of domestic violence. The results from this study, in combination with the results from previous animal studies, suggest that both low 5-HT and high testosterone concentrations can modulate sensory stimuli that serve to activate the neuropathways which mediate fear-induced aggression. These changes predispose perpetrators to overreact to actual as well as perceived threats. Further research, involving a larger subject population, is required to replicate our findings and to determine the mechanism whereby 5-HT and testosterone concentrations differ in perpetrators with and without alcoholism.

References

Albert, D.J., Walsh, M.L., 1982. Medial hypothalamic lesions in the rat enhance reactivity and mouse killing but not social aggression. Physiology and Behavior 28, 791–795.

Albert, D.J., Walsh, M.L., Jonik, R.H., 1993. Aggression in humans: what is its biological foundation? Neuroscience and Biobehavioral Reviews 17, 405–425.

Armony, J.L., LeDoux, J.E., 1997. How the brain processes emotional information. Annals of the New York Academy of Sciences 821, 259–270.

Ballenger, J.C., Goodwin, F.K., Major, L.F., Brown, G.L., 1979. Alcohol and central serotonin metabolism in man. Archives of General Psychiatry 36, 224–227.

Bonson, K.R., Winter, J.C., 1992. Reversal of testosterone-induced dominance by the serotonergic agonist quipazine. Pharmacology, Biochemistry and Behavior 42, 809–813.

Borg, S., Kvande, H., Liljeberg, P., Mossberg, D., Valvenius, P., 1985. 5-Hydroxyindolacetic acid in cerebrospinal fluid in alcoholic patients under different clinical conditions. Alcohol 2, 415–418.

Brown, G., Ballenger, J., Minichiello, M., Goodwin, F., 1979. Human aggression and its relationship to cerebrospinal fluid 5-hydroxyindoleacetic acid, 3-methoxy-4-hydroxyphenylglycol and homovanillic acid. In: Sandler, M. (Ed.), Psychopharmocology of Aggression. Raven Press, New York, pp. 131–148.

Buss, A.H., Durkee, A., 1957. An inventory for assessing different kinds of hostility. Journal of Consulting Psychology 21, 343–349.

Chamberlain, B., Ervin, F.R., Pihl, R.O., Young, S.N., 1987. The effect of raising or lowering tryptophan levels on aggression in vervet monkeys. Pharmacology, Biochemistry and Behavior 28, 503–510.

Cherek, D.R., Lane, S.D., 1999. Effects of D,L-fenfluramine on aggressive and impulsive responding in adult males with a history of conduct disorder. Psychopharmacology 146, 473–481.

Clancy, A.N., Whitman, C., Michael, R.P., Albers, H.E., 1994. Distribution of androgen receptor-like immunoreactivity in the brains of intact and castrated male hamsters. Brain Research Bulletin 33, 325–332.

Cleare, A.J., Bond, A.J., 1995. The effect of tryptophan depletion and enhancement on subjective and behavioural aggression in normal male subjects. Psychopharmacology 118, 72–81.

Coccaro, E.F., Kavoussi, R.J., 1997. Fluoxetine and impulsive aggressive behavior in personality-disordered subjects. Archives of General Psychiatry 54, 1081–1088.

Davis, M., 1997. Neurobiology of fear responses: the role of the amygdala. Journal of Neuropsychiatry and Clinical Neurosciences 9, 382–402.

Davis, M., 1998. Are different parts of the extended amygdala involved in fear versus anxiety? Biological Psychiatry 44, 1239–1247.

Davis, M., Strachan, D., Kass, E., 1980. Excitatory and inhibitory effects of serotonin on sensorimotor reativity measured with acoustic startle. Science 209, 521–523.

Doudet, D., Hommer, D., Higley, J.D., Andreason, P.J., Moneman, R., Suomi, S.J., Linnoila, M., 1995. Cerebral glucose metabolism, CSF 5-HIAA levels and aggressive behavior in

Rhesus monkeys. American Journal of Psychiatry 152, 1782–1787.

Ehrenkranz, J., Bliss, E., Sheard, M.H., 1974. Plasma testosterone: correlation with aggressive behavior and social dominance in man. Psychosomatic Medicine 36, 469–475.

Fava, M., Rosenbaum, J.F., McCarthy, M., Pava, J., Steingard, R., Bless, E., 1991. Anger attacks in depressed outpatients and their response to fluoxetine. Psychopharmacology Bulletin 27, 275–279.

Fink, G., Sumner, B., Rosie, R., Wilson, H., McQueen, J., 1999. Androgen actions on central serotonin neurotransmission: relevance for mood, mental state and memory. Behavioural Brain Research 105, 53–68.

Finley, S.K., Kritzer, M.F., 1999. Immunoreactivity for intracellular androgen receptors in identified subpopulations of neurons, astrocytes and oligodendrocytes in primate prefrontal cortex. Journal of Neurobiology 40, 446–457.

George, D.T., Hibbeln, J.R., Ragan, P.W., Umhau, J.C., Phillips, M.J., Doty, L., Hommer, D., Rawlings, R.R., 2000. Lactate-induced rage and panic in a select group of subjects who perpetrate acts of domestic violence. Biological Psychiatry 47, 804–812.

Greco, B., Edwards, D.A., Michael, R.P., Clancy, A.N., 1996. Androgen receptor immunoreactivity and mating-induced Fos expression in forebrain and midbrain structures in the male rat. Neuroscience 75, 161–171.

Griffiths, P.J., Littleton, J.M., Ortiz, A., 1974. Changes in monoamine concentrations in mouse brain associated with ethanol dependence and withdrawal. British Journal of Pharmacology 50, 489–498.

Hashimoto, S., Inoue, T., Koyama, T., 1999. Effects of conditioned fear stress on serotonin neurotransmission and freezing behavior in rats. European Journal of Pharmacology 378, 23–30.

Higley, J.D., Mehlman, P.T., Poland, R.E., Taub, D.M., Vickers, J., Suomi, S.J., Linnoila, M., 1996. CSF testosterone and 5-HIAA correlate with different types of aggressive behaviors. Biological Psychiatry 40, 1067–1082.

Higley, J.D., Mehlman, P.T., Taub, D.M., Higley, S.B., Suomi, S.J., Linnoila, M., Vickers, J.H., 1992. Cerebrospinal fluid monoamine and adrenal correlates of aggression in free-ranging rhesus monkeys. Archives of General Psychiatry 49, 436–441.

Hollingshead, A., Redlich, F., 1958. Social Class and Mental Illness. Wiley, New York.

Inoue, T., Tsuchiya, K., Koyama, T., 1996. Serotonergic activation reduces defensive freezing in the conditioned fear paradigm. Pharmacology, Biochemistry and Behavior 53, 825–831.

Irwin, M., Dreyfus, E., Baird, S., Smith, T.L., Schuckit, M., 1988. Testosterone in chronic alcoholic men. British Journal of Addiction 83, 949–953.

Kaneyuki, T., Morimasa, T., Okada, H., Shohmori, T., 1991. The effect of acute and repeated ethanol administration on monoamines and their metabolites in brain regions of rats. Acta Medicinae Okayama 45, 201–208.

Kantor, G.K., Straus, M.A., 1990. The 'drunken bum' theory of wife beating. In: Straus, M.A., Gelles, R.J. (Eds.), Physical Violence in American Families. Transaction Publishers, New Brunswick, NJ, pp. 203–224.

Katz, R.J., Thomas, E., 1976. Effects of para-chlorophenylalanine upon brain stimulated affective attack in the cat. Pharmacology, Biochemistry and Behavior 5, 391–394.

LaBar, K.S., Gatenby, J.C., Gore, J.C., LeDoux, J.E., Phelps, E.A., 1998. Human amygdala activation during conditioned fear acquisition and extinction: a mixed-trial fMRI study. Neuron 20, 937–945.

LeDoux, J.E., 1998. Fear and the brain: where have we been and where are we going? Biological Psychiatry 44, 1229–1238.

LeDoux, J.E., Cicchetti, P., Xagorasis, A., Romanski, L.M., 1990. The lateral amygdaloid nucleus: sensory interface of the amygdala in fear conditioning. Journal of Neuroscience 10, 1062–1069.

Lidberg, L., Tuck, J.R., Åsberg, M., Scalia-Tomba, G.P., Bertilsson, L., 1985. Homicide, suicide and CSF 5-HIAA. Acta Psychiatrica Scandinavica 71, 230–236.

Limson, R., Goldman, D., Roy, A., Lamparski, D., Ravitz, B., Adinoff, B., Linnoila, M., 1991. Personality and cerebrospinal fluid monoamine metabolites in alcoholics and controls. Archives of General Psychiatry 48, 437–441.

Marks, G.A., Speciale, S.G., Cobbey, K., Roffwarg, H.P., 1987. Serotonergic inhibition of the dorsal lateral geniculate nucleus. Brain Research 418, 76–84.

Mattsson, A., Schalling, D., Olweus, D., Low, H., Svensson, J., 1980. Plasma testosterone, aggressive behavior and personality dimensions in young male delinquents. Journal of the American Academy of Child Psychiatry 19, 476–490.

Mehlman, P.T., Higley, J.D., Faucher, I., Lilly, A.A., Taub, D.M., Vickers, J., Suomi, S.J., Linnoila, M., 1994. Low CSF 5-HIAA concentrations and severe aggression and impaired impulse control in nonhuman primates. American Journal of Psychiatry 151, 1485–1491.

Moeller, F.G., Dougherty, D.M., Swann, A.C., Collins, D., Davis, C.M., Cherek, D.R., 1996. Tryptophan depletion and aggressive responding in healthy males. Psychopharmacology 126, 97–103.

Morgan, M.A., LeDoux, J.E., 1995. Differential contribution of dorsal and ventral medial prefrontal cortex to the acquisition and extinction of conditioned fear in rats. Behavioral Neuroscience 109, 681–688.

Morrison, J.H., Foote, S.L., 1986. Noradrenergic and serotoninergic innervation of cortical, thalamic and tectal visual structures in old and new world monkeys. Journal of Comparative Neurology 243, 117–138.

Murphy, A.Z., Shupnik, M.A., Hoffman, G.E., 1999. Androgen and estrogen (alpha) receptor distribution in the periaqueductal gray of the male rat. Hormones and Behavior 36, 98–108.

Olweus, D., Mattsson, A., Schalling, D., Low, H., 1980. Testosterone, aggression, physical and personality dimensions in normal adolescent males. Psychosomatic Medicine 42, 253–267.

Olweus, D., Mattsson, A., Schalling, D., Low, H., 1988. Circulating testosterone levels and aggression in adolescent males: a causal analysis. Psychosomatic Medicine 50, 261–272.

Polinsky, R.J., Brown, R.T., Burns, R.S., Harvey-White, J., Kopin, I.J., 1988. Low lumbar CSF levels of homovanillic acid and 5-hydroxyindoleacetic acid in multiple system atrophy with autonomic failure. Journal of Neurology, Neurosurgery and Psychiatry 51, 914–919.

Pope, H.G., Katz, D.L., 1990. Homicide and near-homicide by anabolic steroid users. Journal of Clinical Psychiatry 51, 28–31.

Pope, H.G.J., Kouri, E.M., Hudson, J.I., 2000. Effects of supraphysiologic doses of testosterone on mood and aggression in normal men. Archives of General Psychiatry 57, 133–140.

Rahe, R.H., Karson, S., Howard, N.S., Rubin, R.T., Poland, R.E., 1990. Psychological and physiological assessments on American hostages freed from captivity in Iran. Psychosomatic Medicine 52, 1–16.

Reeves, A.G., Plum, F., 1969. Hyperphagia, rage and dementia accompanying a ventromedial hypothalamic neoplasm. Archives of Neurology 20, 616–624.

Reisine, T., Soubrie, P., Artaud, F., Glowinski, J., 1982. Sensory stimuli differentially affect in vivo nigral and striatal [3H] serotonin release in the cat. Brain Research 232, 77–87.

Roy, A., Adinoff, B., Linnoila, M., 1988. Acting out hostility in normal volunteers: negative correlation with levels of 5HIAA cerebrospinal fluid. Psychiatry Research 24, 187–194.

Ruusa, J., Bergman, B., Sundell, M., 1997. Sex hormones during alcohol withdrawal: a longitudinal study of 29 male alcoholics during detoxification. Alcohol and Alcoholism 32, 591–597.

Salzman, C., Wolfson, A.N., Schatzberg, A., Looper, J., Henke, R., Albanese, M., Schwartz, J., Miyawaki, E., 1995. Effect of fluoxetine on anger in symptomatic volunteers with borderline personality disorder. Journal of Clinical Psychopharmacology 15, 23–29.

Shaikh, M.B., Barrett, J.A., Siegel, A., 1987. The pathways mediating affective defense and quiet biting attack behavior from the midbrain central gray of the cat: an autoradiographic study. Brain Research 437, 9–25.

Shaikh, M.B., Brutus, M., Siegel, H.E., Siegel, A., 1985. Topographically organized midbrain modulation of predatory and defensive aggression in the cat. Brain Research 336, 308–312.

Shaikh, M.B., De Lanerolle, N.C., Siegel, A., 1997. Serotonin 5-HT1A and 5-HT2/1C receptors in the midbrain periaqueductal gray differentially modulate defensive rage behavior elicited from the medial hypothalamus of the cat. Brain Research 765, 198–207.

Shaikh, M.B., Siegel, A., 1994. Neuroanatomical and neurochemical mechanisms underlying amygdaloid control of defensive rage behavior in the cat. Brazilian Journal of Medical Biological Research 27, 2759–2779.

Siegel, A., Roeling, T.A.P., Gregg, T.R., Kruk, M.R., 1999. Neuropharmacology of brain-stimulation-evoked aggression. Neuroscience and Biobehavioral Reviews 23, 359–389.

Soler, H., Vinayak, P., Quadagno, D., 2000. Biosocial aspects of domestic violence. Psychoneuroendocrinology 25, 721–739.

Spielberger, C.D., Gorsuch, R.L., Lushene, R.D., 1970. Test Manual for the State-Trait Anxiety Inventory. Consulting Psychologists Press, Palo Alto, California.

Spitzer, R.L., Williams, J.B.W., Gibbon, M., First, M.B., 1992. The Structured Clinical Interview for DSM-III-R (SCID). I: History, rationale and description. Archives of General Psychiatry 49, 624–629.

Spoont, M.R., 1992. Modulatory role of serotonin in neural information processing: implications for human psychopathology. Psychological Bulletin 112, 330–350.

Statsoft, 1994. Statistica for Windows (volume I-III). Statsoft, Inc, Tulsa.

Statsoft, 1999. Statistica'99 Edition. StatSoft, Inc, Tulsa.

Straus, M.A., 1979. Measuring intrafamily conflict and violence: the conflict tactics (CT) scales. Journal of Marriage and the Family 41, 75–88.

Straus, M.A., 1990. Measuring intrafamily conflict and violence: the conflict tactics (CT) scales. In: Straus, M.A., Gelles, R.J. (Eds.), Physical Violence in American Families. Transaction Publishers, New Brunswick, NJ, pp. 29–47.

Straus, M.A., Gelles, R.J., 1986. Societal change and change in family violence from 1975 to 1985 as revealed by two national surveys. Journal of Marriage and the Family 48, 465–479.

Stutzman, G.E., McEwen, B.S., LeDoux, J.E., 1998. Serotonin modualtion of sensory inputs to the lateral amygdala: dependency on corticosterone. Journal of Neuroscience 18, 9529–9538.

Su, T., Pagliaro, M., Schmidt, P.J., Pickar, D., Wolkowitz, O., Rubinow, D.R., 1993. Neuropsychiatric effects of anabolic steroids in male normal volunteers. Journal of the American Medical Association 269, 2760–2764.

Tonkonogy, J.M., Geller, J.L., 1992. Hypothalamic lesions and intermittent explosive disorder. Journal of Neuropsychiatry and Clinical Neurosciences 4, 45–50.

Valzelli, L., Bernasconi, S., Garattini, S., 1981. *p*-Chlorophenylalanine-induced muricidal aggression in male and female laboratory rats. Neuropsychobiology 7, 315–320.

Viana, M.B., Graeff, F.G., Loschmann, P.A., 1997. Kainate microinjection into the dorsal raphe nucleus induces 5-HT release in the amygdala and periaqueductal gray. Pharmacology, Biochemistry and Behavior 58, 167–172.

Virkkunen, M., Nuutila, A., Goodwin, F.K., Linnoila, M., 1987. Cerebrospinal fluid monoamine metabolite levels in male arsonists. Archives of General Psychiatry 44, 241–247.

Virkkunen, M., DeJong, J., Bartko, J., Goodwin, F.K., Linnoila, M., 1989a. Relationship of psychobiological variables to recidivism in violent offenders and impulsive fire setters. Archives of General Psychiatry 46, 600–603.

Virkkunen, M., DeJong, J., Bartko, J., Linnoila, M., 1989b. Psychobiological concomitants of history of suicide at-

tempts among violent offenders and impulsive fire setters. Archives of General Psychiatry 46, 604–606.

Virkkunen, M., Kallio, E., Rawlings, R., Tokola, R., Poland, R.E., Guidotti, A., Nemeroff, C., Bissette, G., Kalogeras, K., Karonen, S.L., Linnoila, M., 1994a. Personality profiles and state aggressiveness in Finnish alcoholic, violent offenders, fire setters and healthy volunteers. Archives of General Psychiatry 51, 28–33.

Virkkunen, M., Rawlings, R., Tokola, R., Poland, R.E., Guidotti, A., Nemeroff, C., Bissette, G., Kalogeras, K., Karonen, S.L., Linnoila, M., 1994b. CSF biochemistries, glucose metabolism and diurnal activity rhythms in alcoholic, violent offenders, fire setters and healthy volunteers. Archives of General Psychiatry 51, 20–27.

Zeman, W., King, F.A., 1958. Tumors of the septum pellucidum and adjacent structures with abnormal affective behavior: an anterior midline structure syndrome. Journal of Nervous and Mental Disease 127, 490–502.

Zhang, L., Barker, J.L., Rubinow, D.R., 1999. Sex differences in expression of serotonin receptors (subtypes 1A and 2A) in rat brain: a possible role of testosterone. Neuroscience 94, 251–259.