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Tryptophan Depletion, Executive Functions, and Disinhibition in Aggressive, Adolescent Males

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Low serotonin has been associated with aggressive behavior and impulsivity. Executive functions (cognitive abilities involved in the initiation/maintenance of goal attainment) have also been related to aggression. We tested whether dietary depletion of tryptophan, the amino acid precursor of serotonin, would increase disinhibition (impulsivity) in aggressive male adolescents. Cognitive-neuropsychological variables predictive of disinhibition were explored. Stable aggressive and nonaggressive adolescent men received balanced and tryptophan-depleted amino acid mixtures separately (counterbalanced, double-blind). Commission errors on a go/no-go learning task (i.e., failures to inhibit responding to stimuli associated with punishment/nonreward) measured disinhibition. Aggressive adolescent males made more commission errors as compared to nonaggressives. Lower executive functioning was significantly related to commission errors over and above conventional memory abilities. Tryptophan depletion had no effect on commission errors in the aggressive adolescents, possibly because of a ceiling effect.

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KEY WORDS: *Serotonin; Tryptophan; Executive functions; Aggression; Disinhibition; Impulsivity*

Serotonin (5-HT) has been linked to aggressive behavior in animals (Pucilowski and Kostowski 1980) and humans (Kavoussi et al. 1997), although the evidence supporting this relationship has been debated (Berman et al. 1997; Tuinier et al. 1995). Dietary depletion of tryptophan, a method known to lower brain 5-HT synthesis in humans (Nishizawa et al. 1997), increases human aggression in the laboratory (Cleare and Bond 1995; Moeller et al. 1996; Pihl et al. 1995), although the effect is relatively small. Other studies have found no such effect (Salomon et al. 1994; Smith et al. 1987). In clinical samples, studies with adults (Brown et al. 1982) and children (Kruesi et al. 1990) suggest that reduced baseline functioning of the central 5-HT system is associated with aggressive/violent behavior in general, and more specifically with *impulsive* violent behavior (Linnoila et al. 1983; Virkkunen et al. 1994). Thus, at a more fundamental level, 5-HT may be controlling the inhibition of behavior (Soubrié 1986).

Studies investigating the role of 5-HT in impulsive aggression have primarily utilized self-report measures of impulsivity. The first goal of the present study was to test the hypothesis that lowered 5-HT synthesis (and presumably function) might transiently increase behavioral disinhibition measured objectively in the labora-

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tory in a sample of stable aggressive young men who were part of a larger cohort followed longitudinally since the age of five. Disinhibition was defined as behavior committed in the presence of stimuli previously associated with punishment or loss of potential reward, conceptually representing one component of impulsivity. Commission errors on a go/no-go passive avoidance learning task assessed disinhibition; this measure discriminates disinhibited groups from controls (Iaboni et al. 1995; Newman et al. 1985).

The second goal of the present study was to assess the relationship between disinhibition and cognitive functioning in this sample. Cognitive-neuropsychological processes have been implicated in the regulation of aggressive behavior (Pennington and Ozonoff 1996). Specifically, selective deficits in executive functions have been correlated with physical aggression (Séguin et al. 1995). Executive functions subsume the capacities for initiation and maintenance of goal attainment (Lezak 1985). These include the planning of motor skills, modulation of behavior in light of expected future consequences, learning of contingencies, ability to use feedback, abstract reasoning, problem solving, and sustained attention and concentration (Séguin et al. 1995). Given the association between aggression and impulsivity, it was predicted that decreased executive functioning would be associated with increased disinhibition. (In addition to executive functioning, measures of conventional memory processes were also included to account for possible confounds).

METHODS AND MATERIALS

Participants

Participants were selected from a sample of 1,037 17 year-old boys followed since kindergarten (Mâsse and Tremblay 1997). They were classified according to their percentile scores on the teacher-rated physical aggression subscale of the Social Behavior Questionnaire (Tremblay et al. 1991) assessed at ages 6, 10, 11, and 12. Those boys scoring >70th percentile on the aggression subscale at age 6 and at least two of the three additional assessment points were classified as Stable Aggressive (SA). Those scoring <65th percentile were classified as Nonaggressive (NA). A list of 92 potential participants was generated, of which 38 participated in the study (18 SA, 20 NA).

Procedure and Instruments

Demographic Variables. IQ was estimated according to Sattler (1988) using the Vocabulary and Block Design subtests of Weschler Intelligence Scale for Children-Revised (Wechsler 1974) administered at age 15. Self-reported number of years in school, assessed in 1995, was included. Teacher-rated aggression and anxiety represent the average of participants' ratings at ages 6, 10, 11, and 12 on the fighting and anxiety subscales of the Social Behavior Questionnaire (Tremblay et al. 1991). A family adversity index (Tremblay et al. 1991) was constructed using parental age at the birth of the first child, parental education, parental occupational status (Blishen et al. 1987), and family structure, all assessed when the participant was in kindergarten. Participant-reported fathers' and mothers' occupational status (average of 1994 and 1995 assessments) (Blishen et al. 1987) and total family revenue (in 1993) provided a more recent assessment of the participants' family socioeconomic status.

Cognitive/Neuropsychological Variables. At ages 13 and 14 (1991/92), participants were administered a neuropsychological test battery, described previously (Séguin et al. 1995). These tests results were factor analyzed in a larger sample (n=177) (Séguin et al. 1995). Four factors accounting for 58% of the variance were found, including Verbal Learning (composed of the Semantic and Letter Fluency [Lezak 1983], Paired Associates and Digit Span [Wechsler 1987] tests), Incidental Spatial Learning (composed of the Spatial Memory subtests, see Smith and Milner 1981, 1989), and Executive Function (composed of the Nonspatial Conditional Association [Petrides 1990], Number Randomization [Wiegersma et al. 1990], Self-Ordered Pointing [Milner et al. 1985], and Strategic Problem Solving [Becker et al. 1986] tests). Participants' scores on these three factors were used in the present study to assess cognitive-neuropsychological correlates of disinhibition on the go/no-go task. Verbal and spatial learning were included to assess conventional memory processes (Séguin et al. 1995).

Acute Tryptophan Depletion. Prospective participants were mailed an information sheet outlining the study, and parental and participant consent forms. Those boys interested in participating were asked to sign the consent form and to obtain parental consent. They were scheduled for the first lab test day, and asked to avoid consumption of certain foods high in protein (e.g., meats), abstain from alcohol and/or recreational drug use the day before each lab session, and refrain from eating breakfast on test days.

A 2 (group; SA, NA) × 2 (amino acid administration; tryptophan depletion [T-] and balanced amino acid mixture [B]) between-/within-subjects design was employed. Each participant was tested on 2 days, separated by at least 1 week. On each day, participants consumed an amino acid mixture administered double-blind. Assignment to order of amino acid administration (T- and B, or B and T-) was counterbalanced within groups. Research assistants who administered the amino acid mixtures, tests, questionnaires, and other procedures were blind to the young mens' behavior ratings.

One or two participants were scheduled per test day. Early in the morning, the boys were transported by car from their homes to the laboratory. Testing commenced at approximately 9:00 A.M. Upon arrival at the lab, adherence to the previous day's specified menu and the prohibitions against recreational drug/alcohol use and breakfast consumption were assessed (by means of self-report). Next, 10 milliliters (ml) of venous blood was drawn from each participant to obtain a measure of pretreatment plasma total and free (nonalbumin-bound) tryptophan levels.

Amino Acid Administration. The T- amino acid mixture was the same as that employed by Benkelfat et al. (1994). The B mixture contained the same amino acids plus 2.3 g L-tryptophan. The amino acids were combined with 150 ml orange juice and 0.8 g artificial sweetener (sodium cyclamate) to improve taste. An alternate combination consisting of 150 ml water and 40 ml chocolate syrup (in lieu of the orange juice) was offered to guard against the development of a conditioned taste aversion. Participants were additionally required to swallow 12 capsules containing three amino acids (4.9 g L-arginine, 2.7 g L-cysteine,and 3.0 g L-methionine) not included in the mixture because of their bitter taste. They were allowed water ad libitum to accomplish this. Chewing gum was provided to participants to remove the aftertaste.

Immediately following amino acid administration, on the first test day only, paper-and-pencil questionnaires measuring various personality dimensions were administered. Participants were weighted. A 5 hour wait period was implemented following the completion of amino acid consumption. This time period has been shown to result in significant declines in plasma free and total tryptophan (Benkelfat et al. 1994) and brain serotonin synthesis (Nishizawa et al. 1997), as well as in behavioral changes (Benkelfat et al. 1994; LeMarquand et al. 1997). During the waiting period, participants were allowed to read or watch one or two movies. They were prohibited from sleeping. Five hours after amino acid administration, a second 10 ml blood sample was drawn from each participant for analysis of the effects of the amino acid mixtures on plasma tryptophan levels.

Assessment of Disinhibition: The Go/No-Go Task. Participants were required to learn, by trial-and-error, to respond (press a button) to "active" stimuli (two-digit numbers paired with reward) and withhold responses to "passive" stimuli (two-digit numbers paired with punishment). For the first session, eight numbers (four active, four passive) were repeated 10 times in different, randomized orders for a total of 80 trials. For the second session, 10 different numbers (five active, five passive) were repeated eight times in randomized orders, again for a total of 80 trials. Four different sets of stimuli were employed per session, one for each condition. Additional characteristics of the stimuli have been presented elsewhere (Newman and Kosson 1986).

Visual, auditory, and monetary feedback followed each response. Correct responses were rewarded with a high-pitched tone, presentation of the word "CORRECT" on the computer screen, and the addition of 10 cents to a running tally of the participant's earnings presented on screen. Incorrect responses were punished by a low-pitched tone, the word "WRONG," and subtraction of 10 cents from the participant's earnings. Each participant did four conditions of the go/no-go task. In the reward–punishment (Rew–Pun) condition, participants started with one dollar. Responses to active stimuli were rewarded, and responses to passive stimuli punished. In the punishment-only (Pun–Pun) condition, participants began with four dollars and had no opportunity to win more money. Responses to passive stimuli and failures to respond to active stimuli were punished. In the reward-only (Rew-Rew) condition, participants began with no money and could not lose money. Responses to active stimuli and withholding responses to passive stimuli were rewarded. In the final punishment-reward (Pun–Rew) condition, participants started with one dollar; failures to respond to active stimuli were punished, and nonresponses to passive stimuli were rewarded. Each condition was preceded by a reward pretreatment (12 [first session] or 15 [second session] trials presented in the format described above with the frequency of active and passive stimuli in the ratio of 2:1) before the standard 80 trials of the condition. This pretreatment served to establish a dominant response set for reward (Newman et al. 1990).

Participants received instructions concerning the nature of go/no-go task, the reinforcement contingencies, and the process of trial-and-error learning. In the presence of the experimenter, they received eight practice trials involving four presentations of each of two practice stimuli (01 as an active stimulus; 02 as a passive stimulus). The experimenter answered any questions the participant had, but was not present during actual testing. Participants were randomly assigned to one of the 24 possible orders of presentation of the four conditions. At the conclusion of each condition, the experimenter re-entered the room to explain the demands of the next condition. Dependent measures for this task included commission errors (failures to inhibit responses to passive stimuli) and omission errors (failures to respond to active stimuli) for each condition.

Tryptophan Repletion. Following completion of the go/no-go task, participants were provided with a high-protein snack and a 1 g L-tryptophan tablet to normalize plasma tryptophan levels if the individual was tryptophan-depleted, or to maintain the double-blind status of the study if the individual received the B amino acid mixture. The tryptophan preparation used (Tryptan) is

available by prescription in Canada and has not been associated with any cases of eosinophilia-myalgia syndrome (Wilkins 1990). One hour following the start of meal consumption, a final 10 ml blood sample was drawn to measure plasma tryptophan concentrations following repletion. Plasma-free tryptophan was measured in all blood samples. This procedure has been fully detailed previously (Benkelfat et al. 1994). The participants were remunerated for their time and given their winnings on the go/no-go task. After completing both amino acid administrations, participants were debriefed. They were provided with an information sheet outlining the basic goals of the study, and any questions were answered.

Data Analysis

Variables were initially inspected by group for normality, homogeneity of variance, and outliers. Appropriate transformations or treatment of outliers were applied to correct for violations of these assumptions (Tabachnick and Fidell 1989), and, where employed, are specified. Demographic characteristics of SA and NA participants were compared using *t*-tests for continuous variables or Fisher's Exact Test (two-tailed) for frequencies. Plasma-free tryptophan levels were analyzed using a 2 (group; SA, NA) × 2 (treatment; T-, B) × 3 (time; pre-, 5 hours post-amino acid consumption, 1 hour postrepletion) between–within analysis of variance (ANOVA). For the go/no-go discrimination task, separate 2 (group) × 2 (treatment) × 4 (condition; Rew–Pun, Pun–Pun, Rew–Rew, Pun–Rew) mixed-model ANOVAs were performed on omission and commission errors. Statistically significant interactions were further analyzed using simple interaction effects tests followed by pairwise comparisons using the Newman–Keuls procedure. Geisser–Greenhouse corrections were used for all main effects and interactions involving repeated measures. Relationships between cognitive/neuropsychological functioning and disinhibition on the go/no-go were explored using multiple regression.

Ethical Approval

All participants involved in this study, as well as their parents, gave written informed consent. The study was approved by the Research Ethics Board of the Department of Psychiatry, McGill University.

RESULTS

Six participants (three SA, three NA) completed only one of the two amino acid test days. Go/no-go data for the missing test day for these participants was estimated using group means. Additionally, three participants (one SA, two NA), who completed both amino acid test days, came for cognitive testing at age 13 but not at age 14. Missing test scores on two factors (verbal learning and executive function) were estimated using multiple regression to predict missing test data within each factor, then multiplying the predicted test scores by the factor weights to estimate the factor scores. All analyses reported below were rerun omitting participants with missing data; the results were not different.

Three NA and two SA participants vomited during one of the test days, were retained for testing on that day, and subsequently completed the entire experiment. In four cases, emesis occurred during the T- amino acid session. The analyses below were rerun omitting the participants who vomited during the T- session; again the results were not different.

Demographic Data

Demographic characteristics of the study sample are presented in Table 1. SA participants had lower estimated IQs [t (23.14) = -2.90, p = .008], fewer years of education [t (17) = -3.42, p = .003], lower family revenues in 1993 [t (36) = -2.17, p = .037], and higher (square root) teacher-rated averaged aggression [t (36) = 19.62, $p < .001$] and averaged anxiety [t (36) = 2.94, p = .006].

Comparisons between those SA participants tested (n=38) versus those not tested (n=54) revealed that those tested were higher in teacher-rated aggression (p=.10) and anxiety [t (35.39) = -2.24, p = .03] than those not tested. In the NA group, those tested were no different in aggression or anxiety compared to those not tested.

Table 1. Demographic Characteristics of Stable Aggressive (SA) and Nonaggressive (NA) Participants[a]

Measure (Year of Assessment)	SA	NA
Number	18	20
Age, years	17.2 ± 0.4	17.0 ± 0.6
Weight, lb	158 ± 36.9	147 ± 17.1
IQ, (WISC—R short form)[b]	93 ± 14.9	104 ± 6.7**
Education, years (1995)	10.3 ± 0.9	11.0 ± 0.0**
Teacher-rated aggression	2.9 ± 0.9	0.1 ± 0.1**
Teacher-rated anxiety	4.8 ± 1.7	2.9 ± 2.1**
Family adversity (1984)	0.4 ± 0.2	0.4 ± 0.2
Family revenue (1993)	5.8 ± 2.7	8.0 ± 3.4*
Mother's occupational prestige (1994–95)	34.1 ± 6.9	38.1 ± 11.6
Father's occupational prestige (1994–95)	40.9 ± 10.2	46.2 ± 11.3

[a]Values represent raw data and are expressed as mean ± standard deviation.
[b]WISC—R, Weschler Intelligence Scale for Children—Revised.
*$p < .05$; **$p < .01$.

Serum Free and Total Tryptophan Levels

Plasma free tryptophan concentrations were square root transformed to correct for positive skewness and violations of the homogeneity of variance assumption. Analysis of plasma free tryptophan concentrations revealed a highly significant treatment by time interaction [Geisser–Greenhouse F (1.11,39.80) = 28.47, $p < .001$]. The T- amino acid mixture significantly decreased; whereas the B mixture significantly increased, plasma free tryptophan levels 5 hours postconsumption across groups. The T- mixture led to a decline in plasma free tryptophan of 81% across groups; whereas, the B mixture lead to, on average, a 95% increase in plasma free tryptophan concentration. In those four individuals (1 SA, 3 NA) who vomited in the T- session and were retained for testing, plasma total and free tryptophan dropped 64.8 and 48.2%, respectively.

Consumption of the snack and the 1 g tryptophan supplement led to a 353% increase in plasma free tryptophan in the B condition and a 269% increase in the T- condition relative to pre-amino acid administration levels (see Table 2). Levels of total and free tryptophan were significantly lower in those who received the T- mixture as compared to the B mixture following repletion.

Go/No-Go Task

Errors (omission and commission) were summed separately across the 80 trials within each condition. Square root transformations were applied to normalize the positively skewed distributions of the omission and commission errors. Analysis of square root commission errors revealed significant group [F (1,36) = 8.96, $p = .005$] and condition [Geisser–Greenhouse F (2.67,96.07) = 5.07, $p < .01$] main effects. SA participants made more (square root) commission errors as compared to NA participants, and all participants made fewer (square root) commission errors in the Rew–Pun condition relative to the Pun–Rew condition. No main effects or interactions involving treatment were significant, indicating that tryptophan depletion had no effect on square root commission errors by group or condition (see Figure 1).

Analysis of square root omission errors revealed a significant group × treatment × condition interaction [Geisser–Greenhouse F (2.81,101.15) = 3.51, $p = .02$] (see Figure 1). Further analysis revealed a significant group × treatment interaction in the Rew–Pun condition [F (1,36) = 5.66, $p < .03$]; however, post-hoc testing revealed no significant differences between the means.

Square root omission and commission errors were reanalyzed (separately) using estimated IQ, years of education, family revenue, and average teacher-rated anxiety as covariates in separate analyses of covariance (ANCOVAs). In the analyses of square root omission errors, none of the covariates altered the significant group X treatment X condition interaction. In the analyses of square root commission errors, estimated IQ was a marginally significant covariate [F (1,35) = 4.04, $p = .052$], reducing the group main effect to a trend [F (1,35) = 3.56, $p = .068$]. Average teacher-rated anxiety was a significant covariate [F (1,35) = 6.22, $p = .02$], similarly reducing the group main effect to a trend [F (1,35) = 3.16, $p = .08$]. Years of education and family revenue were not significant covariates and did not affect the group difference in commission errors.

Go/No-Go and Cognitive Variables: Interrelationships

To explore relationships between disinhibition on the go/no-go task and cognitive functioning, square root

Table 2. Total and Free Plasma Tryptophan Levels (mean ± standard deviation) at Baseline and 5 Hours Following the Ingestion of a Balanced (B) and Tryptophan-Depleted (T−) Amino Acid Load, and Following Tryptophan Repletion, in SA (Stable Aggressive) and NA (Nonaggressive) Participants

	SA (n = 18)		NA (n = 20)	
Time of Blood Draw	**B Mixture**	**T- Mixture**	**B Mixture**	**T- Mixture**
Total Tryptophan				
Baseline, μg/ml	10.8 ± 2.3	11.1 ± 2.9	11.6 ± 2.1	11.6 ± 2.4
5 h Post amino acid mixture, μg/ml	15.6 ± 6.8 (+42.4%)	1.4 ± 0.5 (−87.0%)	18.9 ± 3.1 (+65.8%)	2.0 ± 1.5 (−82.1%)
Repletion, μg/ml	25.9 ± 10.9 (+147%)	18.7 ± 13.9 (+78%)	35.3 ± 11.7 (+206%)	26.2 ± 16.3 (+136%)
Free Tryptophan				
Baseline, μg/ml	1.3 ± 0.3	1.5 ± 0.3	1.5 ± 0.4	1.5 ± 0.3
5 h Post amino acid mixture, μg/ml	2.3 ± 1.0 (+76.9%)	0.2 ± 0.1 (−85.3%)	3.0 ± 0.8 (+114%)	0.3 ± 0.3 (−76.9%)
Repletion, μg/ml	5.1 ± 3.0 (+279%)	4.6 ± 3.6 (+220%)	7.3 ± 3.2 (+428%)	5.7 ± 4.7 (+317%)

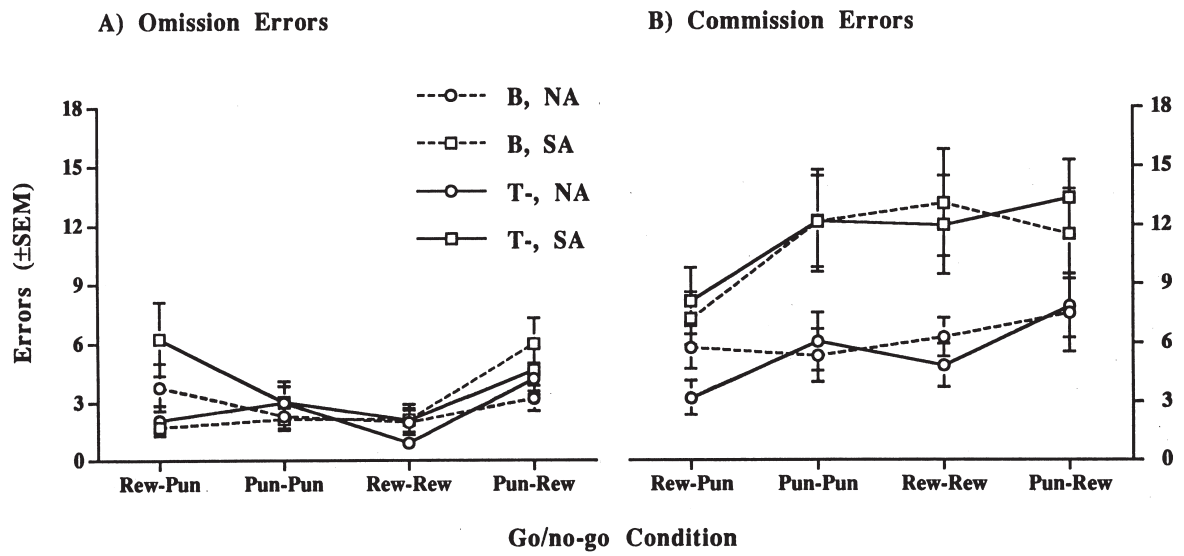

Figure 1. Mean (± standard error) omission and commission errors by condition in each of the two groups following consumption of the two amino acid loads. Rew–Pun indicates the reward–punishment go/no-go condition; Pun–Pun, punishment–punishment; Rew–Rew, reward–reward; Pun–Rew, punishment–reward. T- indicates tryptophan-depleted amino acid mixture; B, balanced amino acid mixture; SA, stable aggressive participants; NA, nonaggressive participants.

omission and commission errors were averaged (separately) across conditions, then treatments, and used as dependent variables in separate multiple regression analyses. Estimated IQ was employed as a measure of general intellectual ability, and the factor scores for the verbal learning, incidental spatial learning, and executive function factors were used as indicators of cognitive functioning. These variables were entered on separate steps, in that order, to test whether executive function was associated with disinhibition over and above IQ, spatial memory, and verbal abilities, the latter two assessing conventional memory processes. Group membership (stable aggressive versus nonaggressive) was added on the last step to see if aggressive status was related to disinhibition over and above cognitive functioning. Executive function significantly predicted average square root commission errors [B (unstandardized) = −0.50, $t = -3.07$, $p = .004$] over and above IQ, spatial memory, and verbal skill. Aggressive group status did not predict (square root) commission errors [B = 0.34, $t = -1.08$, $p = .29$] over and above cognitive functioning. The final equation accounted for 39% of the variance [adjusted R^2; $F(5,32) = 5.72$, $p = .0007$]. Addition of the executive function factor accounted for 21% of the variance in (square root) commission errors over and above the 18% accounted for by estimated IQ and the spatial and verbal factors. Figure 2 shows the relationship between commission errors (by group, averaged across conditions and treatments) and executive function factor scores. None of the cognitive variables, nor group membership, predicted average square root omission errors.

DISCUSSION

The effect of tryptophan depletion on disinhibition (commission errors), and the relationship between executive functions and disinhibition, were investigated in this sample of stable aggressive and nonaggressive adolescent males, a subsample of a larger, well-defined, longitudinal cohort followed for 12 years. First, SA participants made more commission errors than NA participants across go/no-go and amino acid conditions. This finding was robust after controlling for group differences in years of education or family revenue. IQ and teacher-rated anxiety, although significantly related to commission errors, only reduced the group difference marginally. This difference was also not caused by group differences in mood (in general, there were few group or amino acid treatment effects on mood measures [data not shown]).

The group difference in commission errors is congruent with previous work demonstrating increased commission errors (but similar omission errors) in incarcerated psychopaths, extraverts, and juvenile delinquents (Newman and Kosson 1986; Newman et al. 1985, 1990; Patterson et al. 1987) and children with attention deficit hyperactivity disorder (Iaboni et al. 1995). Increased commission errors in psychopaths, extraverts, and juvenile delinquents were found in the reward–punishment condition only (not in the reward–reward or punishment–punishment conditions), leading to the hypothesis that, in situations with competing reward and response cost, a dominant response set for reward is formed making response inhibition difficult when confronted with stimuli associated with response cost

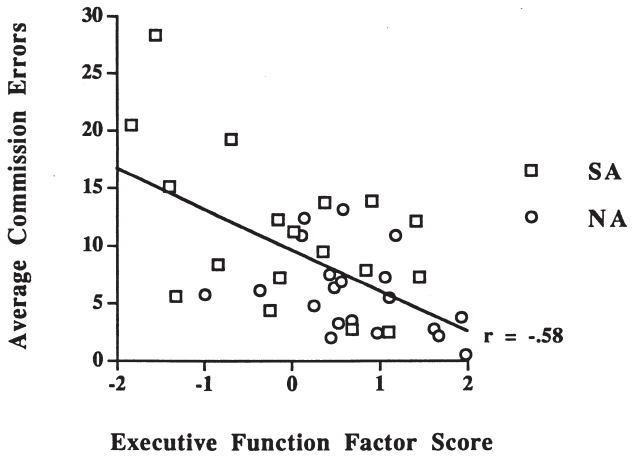

Figure 2. Correlation between commission errors on the go/no-go (averaged across conditions and treatments) and executive function factor scores. SA indicates stable aggressive participants; NA, nonaggressive participants.

(Newman and Wallace 1993). In the present study, commission errors were increased across go/no-go conditions in SA participants (as in attention deficit and hyperactivity disorder children; Iaboni et al.), suggesting a more global impairment in behavioral inhibition in SA young men. Taken together, these studies suggest that disinhibition is an important characteristic of individuals with a history of aggressive behavior.

Two caveats concerning this finding must be noted. First, recent drug use was not formally assessed; the effects of recent drug intoxication and/or withdrawal could have had an impact on passive avoidance learning. Second, participants in the present study and in Iaboni et al. (1995) did all four conditions of the go/no-go; whereas, in other studies (Newman and Wallace 1993), go/no-go conditions were administered between subjects. This procedural change may have an effect on the pattern of results across go/no-go conditions.

The second important finding of the present study is the association between executive functions and commission errors. This association was robust even after controlling for IQ and conventional memory processes, and it accounted for the difference in commission errors between the SA and NA participants, because group membership was no longer associated with commission errors after controlling for executive functions. These results suggest that behavioral disinhibition and reduced executive functioning are correlated and underlie aggressive behavior. Aggressive individuals may have deficits in any combination of abilities tapped by tests of executive function, including learning contingencies or modulating behavior in light of expected future consequences.

Current research supports associations between these variables. Executive functions have been related to aggressive behavior in the laboratory (Giancola and Zeichner 1994; Lau et al. 1995). Neuroimaging studies implicate the dorsolateral prefrontal cortex in the performance of tests measuring executive functions (Petrides et al. 1993a, b). Furthermore, neuropsychological tests associated with areas 9 and 46 of the dorsolateral prefrontal cortex are most associated with physical aggression after controlling for attention deficit hyperactivity disorder and IQ. A recent positron emission tomography (PET) study found that no-go responses (inhibition of thumb flexing) were associated with activation in the right prefrontal cortex (approximately area 46) in healthy males (Kawashima et al. 1996). Future investigation might focus on which specific executive functions and which neuroanatomical areas in the frontal cortex are most highly correlated with commission errors on the go/no-go task.

Tryptophan depletion had no effect on disinhibition on the go/no-go task in aggressive, disruptive young men, in contrast to an earlier study in which tryptophan depletion increased commission errors in young men with family histories of alcoholism (LeMarquand et al. 1997). Although the absence of a tryptophan depletion effect on disinhibition seems to go against the original hypothesis, alternative interpretations should be considered. This result may have been caused by ceiling effects: SA participants made more commission errors as compared to NA participants in the B amino acid condition as well as the T- condition. This suggests that the SA group was disinhibited at baseline (i.e., after the B amino acid mixture), washing out a potential T- effect. Alternatively, the SA group was higher in anxiety compared to: (1) the NA group; and (2) those SA individuals not tested. The presence of anxiety in the SA participants may have mitigated against finding an effect of tryptophan depletion.

Reduced baseline serotonin functioning in aggressive children and adolescents has been suggested in a number of studies (Halperin et al. 1994, 1997; Kruesi et al. 1990, 1992). SA and NA participants did not differ on one possible factor influencing serotonin synthesis—baseline plasma tryptophan levels prior to amino acid administration. Following tryptophan depletion and subsequent repletion, however, plasma tryptophan levels in SA participants were somewhat lower than those of NA participants, possibly suggesting a lag in the availability of tryptophan for 5-HT synthesis in some circumstances. If aggressive young men do have somewhat lower baseline serotonergic functioning, augmenting baseline serotonin function could decrease disinhibition (Coccaro and Kavoussi 1997).

In summary, stable aggressive adolescent males were more disinhibited (i.e., made more commission errors) as compared to nonaggressive young men on a go/no-go task. Moreover, executive functions accounted for a significant proportion of the variance in commission er-

rors in the entire sample, over and above IQ, memory abilities, and group membership (stable aggressive vs. nonaggressive). Tryptophan depletion had no effect on disinhibition in stable aggressive young men, possibly because of a ceiling effect.

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