Plasma Endorphin Levels in Pathological Gambling

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Despite its formal definition as a disorder of impulse control, pathological gambling has come under the generic label of addictive disorders with subjective excitement and physiological arousal as the major motivating factor. Individual differences in autonomic/cortical arousability in interaction with irregular schedules of reinforcement have been postulated to be important determinant factors in the pathogenesis of pathological gambling (Anderson & Brown, 1984). Mood disturbances and cross-addictions are frequently observed in pathological gamblers seeking treatment and the behavior has also been conceptualized as a defense against depression and anxiety. Recently the role of endorphins has been implicated in mood disturbances associated with psychiatric states and in addictive processes; the latter through their euphorogenic or reward-transmitting properties in accordance with operant and classical conditioning principles. The hypothesis that the etiology or maintenance of gambling behavior is related to endorphin activity was investigated in this study. Using radioimmunoassay techniques, baseline B-endorphin plasma levels were measured in a sample of 39 pathological gamblers seeking treatment and 16 male and 19 female non-gambling healthy control subjects. In addition, B-endorphin reactivity to gambling activity was measured in a subgroup of 13 horse-race gamblers.

Diagnostic and Statistical Manual III criteria for diagnosis were used. Written consent was obtained. Blood samples were drawn at the same time of day for each subject. The experimental procedure consisted of taking baseline blood samples at 11 a.m. following which subjects were instructed to place a bet sufficient to "excite" them on a horse-race. A subsequent blood sample was taken at 2 p.m., five minutes after subjects listened to the race broadcast on radio. Heart rate measures and a visual analogue scale rating excitement, tension and urge to gamble were also administered immediately before and after the race broadcast. Results showed that as a group pathological gamblers did not differ from controls on baseline B-endorphin levels.

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But differentiating gamblers according to type of gambling activity revealed horse-race addicts to have significantly lower baseline levels as compared to poker-machine players and controls. This finding provides empirical evidence for the hypothesis that distinct subgroups of gamblers exist and raises the corollary that different etiological factors may characterize each subgroup. That B-endorphin levels did not increase in response to gambling was explained by the failure of the relatively small bet size to generate high arousal.

INTRODUCTION

Despite Diagnostic and Statistical Manual III (Spitzer, 1980) classifying pathological gambling under the residual category of "Disorders of Impulse Control," there has been a strong trend to regard it as an addictive disorder (Dickerson, 1984; Blaszczynski, Buhrich, & McConaghy, 1985) with many features found in drug and alcohol addiction including withdrawal symptoms of disturbed mood and/or behavior (Wray & Dickerson, 1981), dependence (Moran, 1970) and tolerance (Dickerson, 1984). In the United States pathological gamblers are treated in alcohol and drug addiction centers. Similar individual and group psychotherapy and education programs are given to these groups and Gamblers Anonymous is modelled on the principles and format of Alcoholics Anonymous.

The experimental analysis of addictive behaviors is strongly affected by Skinner's (1953) operant conditioning paradigm. If pathological gambling is conceptualized as an addictive disorder then similar processes may also be seen to be operating with subjective excitement generated by gambling as the reinforcing factor. Moskowitz (1980) commented "that the thrill and excitement are so pleasurable that they are virtually addicting. . . . It is this charged-up feeling, a mixture of super confidence, enthusiasm, fear, and guilt that seems to drive the patient toward the gaming table."

In the clinical experience of the first author (A.P.B.), gamblers frequently described their excitement as analogous to the euphoric mood state or "fix" experienced by drug addicts. A further observation suggested that the motivation to gamble differed between various forms of gambling. In addition to or because of the excitement of gambling, poker-machine players reported secondary rewards in the form of "psychic or emotional escape" from stress. They became totally oblivious to their daily problems. Horse-race addicts on the other hand more frequently reported that gambling served to reduce dysphoric mood states or boredom. Often they would delay the receipt of race results to prolong anticipatory excitement and arousal. Expectations of large wins which may lead to improved financial and socioeconomic status may also provide current and anticipatory reinforcement value despite continued losses (Tec, 1964).

Skinnerian conditioning theory is inadequate in accounting for all the phenomenology of pathological gambling, particularly relapse after abstinence. Anderson and Brown (1984) and Brown (1984) postulated a model of gambling based on individual differences in autonomic and cortical arousal which, in interaction with irregular reinforcement schedules, led to the development of pathological gambling. Such a neo-Pavlovian model in which physiological arousal plays an important role in the addictive process accounts for the reinstatement process and "allows for the maintenance of the behavior by internal mood/state/arousal cues in addition to external situation cues" (Anderson & Brown, 1984, p. 402).

Little objective data is available to substantiate clinical observation but two empirical studies have shown gambling to be a risk-taking activity that is associated with a high degree of subjective excitement and physiological arousal. Anderson and Brown (1984) found mean heart rate increases of 23.1 beats per minute in response to real-life casino gambling with half their sample of twelve gamblers reporting excitement as their main motivation for gambling. Leary and Dickerson (1984) showed that exposure to gambling cues did not alter baseline arousal in either high or low frequency poker-machine players. Playing was associated with increased arousal in both groups, significantly so for the high frequency players. Their mean heart rate increase of 13.5 beats per minute was lower than that observed by Anderson and Brown (1984) but was most likely accounted for by differences in simulated versus actual gambling conditions and average bet size. Increased subjective ratings of anxiety as measured by a shortened form of the Spielberger's State-anxiety inventory paralleled heart rate increases.

Recently the role of brain neuropeptides have been implicated in the acquisition of addictive behaviors (Goldstein, 1976; Hughes, 1976; Snyder, 1975; Van Ree, 1983). Endogenous endorphins produce effects similar to those of exogenous opioids (e.g., morphine), viz., analgesia, euphoria, and in animals, tolerance and physical dependence. B-endorphin appears to serve the function of protection against pain or excessive stimulation and can act as a reinforcer (Van Ree, DeWied, Bradbury, Hulme, and Smyth, 1976). Belluzzi and Stein (1977) found that electrode-implanted rats displayed a higher rate of self-stimulation to obtain met- and leu-enkephalin than to obtain morphine. Conversely, a dose-related decrease in self-stimulation followed the administration of Naloxone, an opiate antagonist. Van Ree (1983) concluded that B-endorphin exerted control over behavior in a way similar to narcotics and that this could lead the functioning of the organism to become conditional upon these neuropeptides.

Endorphins have also been implicated in alcohol dependence. Davis and Walsh (1970) hypothesized that isoquinolines (alkoloid-like substances formed as a result of the reaction of ethanol and dopamine) were involved in the mechanism underlying alcohol dependence. Blum, Hamilton and Hirsch

(1978) extended this notion to hypothesize a "link" between isoquinolines and opiate and alcohol addiction. An association between gambling and alcoholism has also been reported (Ferrioli & Ciminero, 1981; Jacobs, Pettis & Linda, 1981). McCormick, Russo, Ramirez, and Taber (1984) found 36 percent of a sample of 50 compulsive gamblers abused alcohol.

The purpose of this pilot study was to investigate the hypothesis that arousal is a major factor in the maintenance of pathological gambling and further that the specific neurotransmitter Beta-Endorphin mediates the reinforcing "euphoria." Under this conceptualization, the reinforcing euphoria or "high" associated with gambling is related to endorphin release and that the withdrawal symptoms commensurate with cessation of gambling is related to deficiencies of endorphins.

Some indirect evidence supports the notion of altered levels or functioning of endorphins in compulsive gamblers. Pratt, Maltzman, Hauprich and Ziskind (1982) compared 16 "sociopaths," all of whom were compulsive gamblers, to 14 volunteer controls on a cold pressors test. Results showed the gamblers to be less physiologically responsive to noxious stimuli. These authors claimed indirect support for the belief that differences between controls and sociopaths in endogenous opioids underlied this effect.

METHOD

Subjects were 39 pathological gamblers, three females and 36 males, seeking behavior therapy to reduce their uncontrollable gambling urge and behavior. All met Diagnostic and Statistical Manual III criteria for diagnosis as pathological gamblers. All subjects were medication free, two were alcoholics. All subjects had gambled for several years and were gambling over half their weekly income. Fifteen were heavily into debt with amounts ranging from $14,000 to $60,000, and three had embezzled amounts in excess of $27,000. Twenty-six gambled mainly or exclusively on poker-machines and 13 exclusively on horses, trots or dogs.

Thirty-five subjects, 16 males, and 19 females, who did not gamble more than $5.00 or more than once a week were used as the control group. None were on medication.

Design

To control for diurnal variations in Beta-Endorphin levels, baseline plasma samples for all subjects were collected at 11 a.m. Plasma B-endorphin radioimmunoassay was performed by the Department of Endocrinology using the following extraction method. 10 mls of blood was collected in heparinized (not EDTA) tubes and the plasma separated after spinning. One ml. of the plasma sample was taken and B-endorphin extracted on an anti-B-endorphin affinity column, washed with saline and eluted with hydrochloric acid then neuralized with sodium hydroxide. Radioim-

munoassay was performed on the eluted sample. Separation of bound from free was performed using polyethylene glycol (PEG) linked second antibodies.

Three modifications were carried out to the standard procedure. Tubes were siliconized to achieve non-specific bindings of less than 7 percent compared to that in excess of 20% without siliconization, the 5 pmol/L standards were diluted to produce an additional standard of 2.5 pmol/L and heparinized rather than EDTA tubes were used.

For the experimental procedure thirteen horse race addicts were instructed to place a small bet of $2 to $10 at the betting office on a horse-race and to return to the laboratory where they were to listen to the race broadcast. Immediately prior to and again after the race broadcast a three item visual analogue scale measuring present state levels of tension, excitement and urge to gamble was administered. Heart rate and blood pressure were recorded using a digital sphygmomanometer.

RESULTS

The mean age of the pathological gamblers was 34.1 years (S.D. = 6.6 years) and for the controls, 34.9 years (S.D. = 9.6 years), (Table 1). T-test comparisons showed no significant age differences between male and female controls, poker-machine and horse-race gamblers or between the combined controls and combined gamblers.

Baseline B-endorphin levels for pathological gamblers and controls are shown in Table 2. Male and female control groups did not differ significantly ($t = 1.052$, $df = 23$, N.S.) and therefore these groups were combined.

The combined control group was found not to differ significantly from the pathological gamblers ($t = 1.09$, $df = 72$, n.s.).

The assumption that poker-machine gamblers and horse-race addicts formed a homogeneous group was investigated by comparing B-endorphin levels between these subgroups. Results showed the horse-race addicts tended to have lower B-endorphin levels than poker-machine players but this difference just failed to reach the .05 significance level. The poker-machine ad-

Table 1
Age Data for Pathological Gamblers and Control Subjects

	CONTROLS			PATHOLOGICAL GAMBLERS		
	Males	Females	Combined	Poker Machines	Horse Races	Combined
	N = 16	N = 19	N = 35	N = 26	N = 13	N = 39
Mean (Years)	35.1	34.9	34.9	33.8	34.6	34.1
Standard Deviation	9.5	9.9	9.6	6.3	7.36	6.6

dicts were no different from controls but the horse-race addicts had significantly lower levels ($t = 2.032$, $df = 46$, $p < 0.05$) of B-endorphin.

The "unitary hypothesis" of a single neurotransmitter deficiency in psychopathological states, as John L. Sullivan notes (John L. Sullivan, M.D., personal communication), is considered by most investigators as overly simplistic, given the critical interplay of multiple neurotransmitter systems. It is also possible as he concludes, that an observed deficiency in B-endorphin may represent a secondary "downstream effect" of a more primary biochemical abnormality, and the correlation of plasma B-endorphin levels with the concentration of this neurotransmitter at critical receptor sites is still controversial.

For the horse-race gamblers there was a non-significant trend for B-endorphin levels to increase in response to listening to the race broadcast (Table 3). This increase was accounted for by two alcoholic subjects who showed aberrant baseline and reactive B-endorphin scores. Their levels changed from 10 and 12 pmol/L to 30 and 21 pmol/L respectively. Excluding these scores from analyses revealed that B-endorphin levels did not alter in response to the race broadcast. With these two scores excluded, baseline B-endorphin differences between horse-race addicts and poker-machine players reached significance ($t = 2.596$, $df = 44$, $p < 0.01$).

On the visual analogue scale, gamblers rated themselves as moderately excited, tense and as having a moderate urge to continue gambling (Table 4). These ratings remained unchanged across sessions. Blood pressure recordings were obtained from nine subjects (Table 5). Systolic pressure increased as expected given its relationship to sympathetic activity but this increase did not reach significance. Diastolic pressure showed only a marginal change. Heart rate increased significantly from baseline to post race broadcast levels

Table 2
B-Endorphin Levels for Pathological Gamblers & Control Subjects
(pmol/1)

	CONTROLS			PATHOLOGICAL GAMBLERS		
	Males	Female	Combined	Poker Machines	Horse Race	Combined
	N = 16	N = 19	N = 35	N = 26	N = 13	N = 39
Mean	6.50	5.42	5.91	5.65	3.77*	5.02
Standard Deviation	3.01	3.04	3.06	3.87	3.67	3.86

* P <0.05 Horse Race addicts: Combined Controls.

($t = 2.088$, $df = 20$, $p < 0.05$). The mean change of 10.82 beats per minute for this interval was of a small magnitude but consistent with that reported by Leary and Dickerson (1984). As some studies have shown arousal is correlated with mean bet size, the small bet sizes used in this study probably accounts for the low degree of arousal in subjects. There were no significant correlations between the various indices of arousal. The lack of correlations between physiological, subjective and biochemical scores can be accounted for by the relatively low arousal levels experienced. Low correlations between such measures are often reported in studies on anxiety.

DISCUSSION

Pathological gamblers as a group were found not to differ from controls on the measure of baseline B-endorphin level. But the hypothesis that the etiology or maintenance of pathological gambling was related to endorphin levels was supported in part when gamblers were differentiated according to type of gambling. Results of the study showed that horse-race gamblers had significantly lower levels of B-endorphin as compared to poker-machine players and non-pathological gamblers providing empirical evidence against the assumption that pathological gamblers form a homogeneous group. Excitement or arousal may serve different purposes for horse-race gamblers.

Table 3
B-Endorphins of Pathological Gamblers (Horse Race)
Pre- and Post-Race Broadcast

	Pre-Race Broadcast	Post-Race Broadcast
	N = 13	N = 13
Mean	3.77	6.00 N.S.
Standard Deviation	3.67	9.05
	B-endorphin levels excluding two subjects with aberrant scores.	
	N = 11	N = 11
Mean	2.45	2.44 N.S.
Standard Deviation	1.91	2.06

Horse-race gambling involves a sequence of events requiring greater information processing from reading the form guide, placing a bet, anticipation and listening to race broadcasts as compared to a low skill activity such as poker-machine play.

Horse-race gambling may reduce dysphoric mood or intolerable stress-related tension by elevating B-endorphin levels. Although the evidence is not conclusive (Blaszczynski & Winter, 1984), reduction of depression has been reported following the administration of B-endorphin in psychiatric subjects. In a double-blind crossover placebo controlled study, Gerner, Catlin, Gorelick, Hui and Li (1980) found significant improvement in 10 depressed psychiatric patients two to four hours after B-endorphin treatment as compared to a placebo. McCormick et al. (1984) found a high incidence of affective disorders in their sample of 50 pathological gamblers seeking treatment. Seventy-five percent met Research Diagnostic Criteria for major depressive disorder, fourteen percent reporting premorbid onset of symptomatology.

For poker-machine players on the other hand, the motivation may be related to a coping style which allows temporary escape from stress situations rather than a need to elevate deficient B-endorphin levels.

This proposal is consistent with the observation that a proportion of pathological gamblers have a preference toward one form of gambling. Of 46 gamblers investigated in another study (Blaszczynski, 1983), 43 percent gambled exclusively on horses and 24 percent on poker-machines.

The failure of B-endorphin to show any increase in response to actual

Table 4
Visual Analogue Rating Scales for Gamblers
Pre- and Post-Experiment Times

	N = 11		
	Excitement	Urge to Continue Gambling	Tension
Pre-Mean.	55	41	51
Standard Deviation.	21.73	28.85	25.14
Post-Mean.	54.72	38.63	55.00
Standard Deviation.	34.79	29.67	29.75

gambling behavior was considered to be related to the low levels of subjective and physiological arousal generated by the experimental procedure. Although the gambling was conducted under real conditions, the actual amount gambled by subjects, for ethical reasons, was relatively small compared to their usual bets. Other studies have shown a correlation between arousal and average bet size. Replication is needed using larger bets.

Any comprehensive theory of pathological gambling must be multivariate in nature and account for social influences, cognitive variables and physiological factors.

The proposed model outlined in Figure 1 suggests that for the majority of individuals gambling is recreational, controlled and carried out for its excitement value.

Possible biologically determined deficiencies in B-endorphin level predispose some individuals to respond positively to activities that increase arousal, B-endorphin levels and enhance mood. Early exposure by family members or friends and availability of gambling outlets are variables that act to establish habitual gambling behavior patterns. However, for some the addictive process is almost immediate.

Gambling at a pathological level begins in response to anxiety and/or dysphoric mood that arises as a reaction to inadequate coping strategies or personality characteristics. The drive to maintain an optimal level of arousal or stimulation (Zuckerman, 1979) produces the motivation to correct excess or deficient arousal states. Because of learned associations between gambling

Table 5
Physiological Data for Pathological Gamblers at Baseline
Pre- and Post-Experimental Times

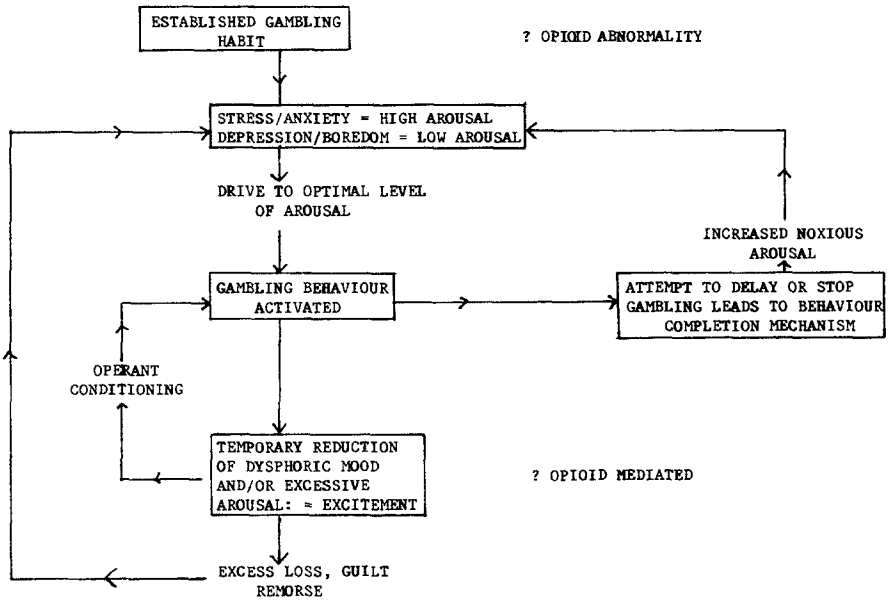
		Baseline	Pre-experimental	Post-experimental
Blood pressure	Mean	118.3	119.12	131.70
Systolic mm/Hg.	Standard Deviation	15.6	11.61	19.51
N = 9				
Blood pressure	Mean	74.33	77.25	81.67
Diastolic mm/Hg.	Standard Deviation	16.77	9.11	16.1
N = 9				
Heart rate(B.P.M)	Mean	69	72.4	79.82
N = 11	Standard Deviation	11.12	9.08	13.1

and excitement, gamblers increase their gambling while reduction of anxiety or depression mediated by B-endorphin activity in one subgroup and by emotional escape in another operates as the positive reinforcement.

The reduction of noxious mood states is only temporary. Financial losses consequent to increased gambling and the guilt, remorse and fear of detection acts to exacerbate dysphoric mood and anxiety maintaining the drive for continued gambling. Bet sizes increase to produce higher levels of arousal and overcome the effects of tolerance. The need to chase losses (Lesieur, 1979) becomes imperative. This secondary process produces the rapid decline into the desperation phase.

Attempts to cease gambling when stimulated to do so at this stage becomes difficult due to the operation of the behavior completion mechanism as described by McConaghy (1980) and McConaghy, Armstrong, Blaszczynski and Allcock (1983). Under this model, once behavior completion mechanisms are established and activated by appropriate cues, failure to complete the behavior results in an increased arousal which the individual experiences as a sense of tension or anxiety and which drives him to complete that behavior.

Figure 1
Pathological Gambling: A Model



The change in arousal leads to an increase in preoccupation and the urge to carry out the compulsive activity. Similarly, Wray and Dickerson (1981) stated "that any repetitive stereotyped behavior that is associated with repeated experiences of physiological arousal or change in arousal . . . may be difficult for the individual to choose to discontinue and should he do so, then it may well be associated with disturbances of mood and behavior."

Alterations in cognitive style may distort self-perceptions and produce cognitive dissonance to accommodate behavior in the desperation phase of compulsive gambling. The belief that restitution can only be achieved by large wins, impatience for rapid restitution and feelings of significant loss or being left in a "void" are variables that maintain the pressure for continued gambling. Cognitions affect emotion and feedback to increase anxiety or dysphoria.

If endogenous opiates have a role in the pathogenesis of pathological gambling then, dependent on whether deficient or excess baseline levels or reactivity of B-endorphin levels are the important consideration, treatments aimed at correcting such biochemical anomolies may be an additional effective approach, especially in severe cases. Opiate antagonists blocking the euphoric effects of gambling may assist in promoting the effectiveness of concurrent treatment strategies.

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