Chapter 4: Research on the Origins of Pathological and Problem Gambling

Etiology is the study of causal pathways. Because of the complex analyses and study designs that must be used, this type of research represents the crown jewel of health research. The outcomes of such research often lead to successful treatments and preventive interventions. The process of discovering causal associations and pathways to understand how different factors, exposures, or disease-causing situations relate to each other usually involves multidisciplinary teams of psychiatrists, psychologists, statisticians, sociologists, economists, and epidemiologists.

This chapter begins by describing considerations for undertaking or evaluating etiological research on pathological gambling, as well as the current state of knowledge regarding the causal pathways of pathological gambling. Risk factors for and correlates of pathological gambling, including psychosocial, environmental, genetic, and biological ones, are discussed and evaluated in terms of commonly accepted criteria for determining the strength of an association. Cooccurring disorders and their similar risk factors are also discussed. Throughout the chapter, substantial deficiencies in current research on pathological gambling are noted.

ETIOLOGICAL CONSIDERATIONS IN UNDERTAKING RESEARCH ON PATHOLOGICAL GAMBLING

Etiological research is complex, and a number of aspects are essential to consider in undertaking it. They include the accuracy of diagnostic labels, the associations and causal relationships among potential risk factors, the uniqueness of risk factors, and age and cohort effects. In order to review the available evidence, the committee developed criteria to determine a causal association between a given risk factor and pathological gambling.

Diagnostic Labels

Considerable discussion has already been devoted to the definition, measurement, and prevalence of pathological gambling. When discussing the etiology of an illness, it is useful to revisit its label, because a label, as suggested by Nathan (1967), reflects the state of knowledge about the illness at the time it is labeled. In addition, etiological explanations keen on identifying causal pathways necessarily take labels into consideration, because they often describe the clinical site and clinical picture of an illness. For example, lung cancer, myocardial infarction, and lymphatic leukemia are medical labels that describe both the clinical site and clinical picture of those illnesses. Medical labels such as tuberculosis and human immunodeficiency virus (HIV) can also specify the diagnosis, cause, or etiology of a physical illness.

Precise diagnostic labels are less common in psychiatry. However, with the American Psychiatric Association's introduction of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), research on the more common mental disorders has flourished and has led to a concomitant explosion in research on risk factors (Goodwin and Guze, 1974). Research on the diagnostic classification of pathological gambling has lagged behind, and it has been identified as an area in serious need of etiological research.

Associations and Causal Relationships

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As with other areas of research, when designing, undertaking, or evaluating etiological research on pathological gambling, one must understand and distinguish between associations and causal relationships among many potential risk factors. A risk factor is something that has a possible role in the initiation of a disease, the progression of a disease to a further state, or in the waning of a disease (which is then a protective factor). Demographic, biological, personality, family, peer, and genetic factors, among other possible risk factors, may interact over time to influence the course of outcomes, symptoms, and behaviors. Risk factors are most useful for research when they refer to a specific phenomenon that provides a feasible point of intervention. Some factors may be related exclusively to initiation; others may be related only to subsequent progression into problem or pathological gambling. Although important, such etiological distinctions have been rarely made in the relatively recent and limited literature on pathological and problem gambling.

The literature on posttraumatic stress disorder (PTSD) offers an analytic model for distinguishing risk factors. Breslau and Davis (1987) demonstrated that it was the original exposure to a precipitating event, and not reexposure, that led to symptoms of PTSD among Vietnam veterans. In another study, Breslau and colleagues (1991), in an examination of young urban adults, identified risk factors for exposure to traumatic events (i.e., low education levels, being male, early conduct problems, and extraversion) that were distinct from risk factors for the actual disorder once exposed (i.e., early separation from parents, neuroticism, preexisting anxiety or depression). Distinguishing risk factors is crucial in etiology research, as is identifying common risk factors for the progression of an illness. In the study just described, a family history of a psychiatric disorder or a substance abuse problem was identified as a common risk factor for exposure to traumatic events and acquiring PTSD.

Unique Risk Factors

Equally important to consider in etiological research on pathological and problem gambling is which factors for chronic, long-term gambling are unique to this disorder and not just predictors of excessive deviant behavior of all kinds. Again, the PTSD literature provides a template for research on pathological and problem gambling. For example, Breslau and Davis (1992) identified several unique risk factors for chronic compared with nonchronic PTSD.

Age and Cohort Effects

Etiological research must also consider how the effects of age and being in a cohort (a group of people born in the same year or decade) increase or decrease one's risk for initiating gambling or developing a gambling problem. Although these effects are infrequently considered in existing pathological and problem gambling research, Erikson's stages of development (Erickson, 1963, 1968, 1982) are one explanatory model that accounts for aging effects and could potentially be applied when investigating gambling behaviors. Specifically, the model hypothesizes that, as people age, they move through several developmental stages that correspond to certain stage-related tasks. When applied to gambling behavior, the implication is that, at certain developmental stages, the motivation for and expectations about gambling might change. A recent review demonstrated that gambling among young people occurs on a developmental continuum of gambling involvement ranging from no gambling experimentation

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to gambling with serious consequences (Stinchfield and Winters, 1998). These effects pertain to how risk factors and outcomes change with age and differ among groups of people (Mok and Hraba, 1991).

Cohort effects pertain to specific events that affect groups of people born during the same time period (Mok and Hraba, 1991). When applied to gambling behavior, this means that increases in gambling opportunities during a certain period in history may affect a certain age group of people. For example, a cohort of same-age people who are passing through the age of risk for gambling problems when gambling opportunities are expanding may experience greater and increasing exposure to, involvement in, and social acceptance of gambling during their lifetimes than a cohort of same-age people at risk during periods of fewer gambling opportunities. In addition, circumstances can affect more than one cohort in the same way or in different ways. A classic example of an event that changed the trajectory of same-age people is the drug revolution of the late 1960s and early 1970s. During this period, expanded drug use affected both teens and young adults, marking this time period as a historical risk factor for drug abuse.

As opportunities to gamble continue to increase throughout most of the United States, it is likely that certain birth cohorts will be affected differently, perhaps in unanticipated ways. For example, in a random telephone survey of 1,011 Iowa residents stratified into eight age cohorts (ranging from 18-24 through 85 and older), it was found, even after controlling for other variables, that older cohorts are less likely to gamble than younger cohorts (Mok and Hraba, 1991).

Criteria to Determine the Strength of an Association

Mindful of the considerations discussed above, and in order to evaluate the research evidence that various risk factors are associated with pathological gambling, the committee adopted a number of general criteria, which are commonly accepted by epidemiologists throughout the world (Hill et al., 1963), for determining the strength of an association:

1. The event or exposure precedes the outcome of pathological gambling;
2. Findings are consistent--that is, they have been replicated in other studies, with other samples, or in other cultures;
3. There is a strong association between the risk factor and pathological gambling;
4. The association between the risk factor and pathological gambling is biologically plausible based on scientific research findings in such areas as behavioral genetics or neurobiology;
5. Findings remain consistent when different study methods and designs are used (e.g., case control and cohort epidemiological studies, experimental studies, biological studies); and
6. Associations examined are specific to pathological gambling and are not generally found in other disorders as well.

To suggest that a causal association might exist between risk factors, events, or situations and pathological gambling, it would be necessary for at least one of these criteria to be met.

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However, satisfying one or more of the criteria would not be sufficient to positively determine if there is a causal relationship between an exposure and pathological or problem gambling. In many gambling studies, the first criterion (that a risk factor necessarily precedes the outcome of pathological or problem gambling) is unknown. Without this principal evidence, an exposure, a situation, or an event is not proven to be causal.

Furthermore, many studies reviewed by the committee collected data without exploring when and to what extent subjects were exposed to potential risk factors, or the age of onset of their pathological or problem gambling. Again from an etiological standpoint, these methodological limitations make it impossible to determine whether suspected risk factors might "cause" pathological or problem gambling, or whether they are only correlated or associated with these behaviors. Thus, much of the evidence presented or implied in the literature as causal to pathological and problem gambling is, by commonly accepted etiological standards, better defined merely as evidence for an association. Still, despite the generally deficient state of etiological research on pathological and problem gambling, there does exist some tangible evidence to suggest certain risk factors and associations.[1]

PSYCHOSOCIAL AND ENVIRONMENTAL RISK FACTORS

Determining psychosocial and environmental risk factors for pathological and problem gambling is guided by the following question: Is the risk for pathological or problem gambling associated with sociodemographic factors, such as age, gender, ethnicity, and family effects, or is it associated with the availability of gambling to the gambler? In this section, we pay special attention to studies having sufficient sample sizes to generalize findings to larger groups within the population and studies that examine: (1) sociodemographic, family, and peer influences that are associated with initiation into gambling, (2) the risk of progression from gambling without problems to problem or pathological gambling, (3) individual factors among multiple factors associated with pathological or problem gambling, and (4) factors that predict chronicity of symptoms of pathological gambling.

Age

In the United States and throughout much of the world, many people begin gambling as children. For example, in a small study of British adolescents ages 13 and 14, the mean age of initiation into gambling for social recreation or entertainment was found to be 8.3 years for boys and 8.9 years for girls (Ide-Smith and Lea, 1988). The literature has also weakly supported a young age of onset of pathological and problem gambling following initiation to gambling (Kallick et al., 1979; Lesieur and Klein, 1987). In a retrospective study, for example, it was found that adult pathological gamblers remembered their gambling addiction to have started when they were between ages 10 and 19 (Dell et al., 1981). In 1990, Griffiths found that adolescents addicted to slot machines began gambling significantly earlier (at 9.2 years of age) than nonaddicted adolescents (who began at 11.3 years of age) (Griffiths, 1990a). In 1997, Gupta and Derevensky (1997) found that pathological gamblers started gambling, on average, at age 10.9 and nonpathological gamblers at age 11.5.

[1] Some demographic risk factors pertaining to pathological and problem gamblers in vulnerable populations were previously discussed in Chapter 3.

Studies of teens indicate that young age of onset of gambling is more than an artifact of reporting bias. According to a summary of five independent studies of high school students conducted between 1984 and 1988 (Jacobs, 1989b; Steinberg, 1988), 36 percent of teenage respondents reported gambling before age 11; 46 percent began gambling between ages 11 and 15; and 18 percent began after age 15. Between 6 and 25 percent of the teenagers in these studies reportedly wanted to stop gambling but could not.

These findings are consistent with a study of 892 eleventh and twelfth graders at four high schools in New Jersey, in which 91 percent reported having gambled during their lifetime and 5.7 percent met criteria for pathological gambling as measured by the DSM-III (Lesieur and Klein, 1987). In a school newspaper survey of over 1,100 students at an inner-city, largely minority Atlantic City high school, 62 percent reported having gambled at area casinos, and 9 percent reported gambling at least once a week (Arcuri et al., 1985). In another study among students from six colleges and universities in New York, New Jersey, Oklahoma, Texas, and Nevada (Lesieur et al., 1991), using the South Oaks Gambling Screen (SOGS), the lifetime gambling rate was found to be 85 percent, the rate of problem gambling was 15 percent and the rate of probable pathological gambling was 5.5 percent (Lesieur and Blume, 1987).[2] Comparable lifetime gambling rates were found in a Minnesota study of 1,094 youths ages 15-18 (including 684 from a random telephone sample and 410 from a school sample) in which the rate of problem gambling was found to be 6.3 percent and the age of onset for over half the subjects was reported to be before or during the sixth grade (Winters et al., 1993). Finally, in a recent review of 12 U.S. and 5 Canadian adolescent gambling studies, Jacobs found that in the past 10 years the number of teenagers ages 12 to 17 reporting serious gambling problems has increased from 50 to 66 percent. The age of onset for gambling has dropped so that now, throughout America, the majority of 12-year-olds have already gambled (Jacobs, in press, WHAT PUBLICATION?).

Studies of those who seek help for themselves or others indicate that gambling severity and frequency varies by age. A recent analysis of problem gambling help-line calls in Texas revealed that the frequency of calls increased with age, peaked at ages 35 to 44, and declined for callers age 45 and older (Cox, 1998). In fact, adults age 55 and older who called about their own gambling problems (14 percent of all callers) were comparable in frequency to those age 18 and younger who called about their own gambling problems (13 percent of all callers). The percentage of calls about a problem gambler from a friend, family member, or other concerned person followed a similar age pattern. Although interesting and clinically meaningful, these help-line data alone do not contradict the notion that younger and older people have gambling problems.

Gender

Etiological studies of pathological and problem gambling have generally focused on men from Gamblers Anonymous (GA) and men from the Veterans Administration hospital system (Mark and Lesieur, 1992). Consequently, men in the general population have been underrepresented in studies, and women are critically underrepresented as well. Many early studies that did include women were based on small numbers of women or relied on anecdotal

[2] The SOGS covers betting for money on a wide variety of gambling activities, including cards, sports, dogs, dice games, bingo, and slot and other machines.

reports of women in Gamblers Anonymous (Lesieur and Blume, 1991). Yet many studies inappropriately generalize findings about men to women (Mark and Lesieur, 1992). Although men typically begin gambling earlier than women, women appear to experience the onset of problem gambling earlier in the course of their gambling disorder than men (Mark and Lesieur, 1992), but controlled studies are rare (Custer, 1982; Livingston, 1974; Custer and Milt, 1985).

The American Psychiatric Association reports in three editions of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) that the rate of pathological gambling is twice as high among men than among women (American Psychiatric Association, 1987, 1994, 1980). Although no epidemiological evidence substantiated this finding at the time the manuals were first published, some studies have found rates that high (e.g., Cunningham-Williams et al., 1998; Volberg and Abbott, 1997; Volberg, 1994), and other studies consistently show that men gamble more and have higher rates of pathological gambling than do women, even if not at twice the rate (e.g., Lesieur et al., 1991).

Ethnicity and Socioeconomic Status

Most studies of pathological and problem gambling have focused on white male gamblers. Consequently, there exists little population-based literature or data pertaining to women or nonwhite ethnic and cultural groups (Mark and Lesieur, 1992; Volberg, 1994). Specifically, studies among black, Hispanic, Asian, and American Indian gamblers have been lacking. The few studies that include diverse populations have in general failed to distinguish the specific racial or ethnic background of the minority group being included, thus limiting conclusions regarding specific subgroups. A few studies have specifically compared gambling among minority and majority populations (Volberg and Abbott, 1997; Zitzow, 1996; Cunningham-Williams et al., 1998). Since the passage of the Indian Gaming Regulatory Act of 1988, gambling among and sponsored by American Indians on reservations has increased substantially (Rose, 1992). In the Zitzow study, American Indian adolescents exhibited more serious problems from gambling, earlier onset of gambling problems, and greater frequency of gambling problems than their non-Indian peers. The Volberg study found that indigenous populations reported more gambling involvement, gambling expenditures, and gambling-related problems than white populations from the same areas. However, the sampling strategies and questionnaires of these two studies were not identical (Volberg and Abbott, 1997). Thus, the Cunningham-Williams et al. study, using a sample of the St. Louis general population, remains one of the few studies of race that controlled for other factors. The finding that problem gambling (but not pathological gambling) is more likely to affect whites than African Americans remains unchallenged. Among African Americans in one study, problem gambling was more common than gambling without problems or social and recreational gambling (Cunningham-Williams et al., 1998).

Studies have also generally failed to disentangle race and ethnicity from issues of poverty and sociodemographic status. A series of analyses of Georgia residents identified 10 sociodemographic variables that correctly discriminated nearly 80 percent of nongamblers from (nonproblematic) social and recreational gamblers; 84 percent of the cases of nongamblers from problem gamblers; and 94 percent of gamblers without problems from pathological gamblers. When compared with nongamblers, problem gamblers tended to be nonwhite (race/ethnicity was not specified), male, and single, and to have low self-esteem (Volberg and Abbott, 1997). An

earlier multistate analysis found that the only significant difference between probable pathological gamblers from different states is that those from the East Coast states and California are significantly more likely to be nonwhite than those from Iowa (Volberg, 1994).

Family and Peer Influences on Children and Adolescents

Family and peer influences on children and adolescents to gamble may also constitute a risk factor for pathological and problem gambling. Studies reveal that gamblers, especially pathological and problem gamblers who begin gambling as children or adolescents, are frequently introduced to gambling by family members or their peers (Jacobs, 1989b, 1989a; Jacobs et al., 1989). Often the first exposure to gambling for American youths is gambling in a relaxed family setting with cards, dice, and board games. Other forms of gambling exposure reported by adolescents include playing lotteries, playing games of skill such as bowling or billiards for money, sports betting, racetrack betting, and gambling in casinos (Lesieur and Klein, 1987; Kuley and Jacobs, 1988; Steinberg, 1988), which themselves may be potentially influenced by family members and friends.

An association between personal gambling and peer gambling has been observed in several studies of adolescent gamblers (Derevensky and Gupta, 1996; Gupta and Derevensky, 1997, 1998; Jacobs, 1989a; Wynne et al., 1996; Stinchfield and Winters, 1998). These findings are consistent with theoretical and empirical literature substantiating that peers have a strong influence on other adolescent risky behaviors, such as substance use, driving without safety belts, and early sexual behavior (Jessor and Jessor, 1977; Kandel, 1985; Billy and Udry, 1985; Newcomb and Bentler, 1989). Moreover, peer gambling may influence an individual's involvement in gambling in a direct way, through social factors that include peer pressure, or through indirect processes, in which an individual is attracted to a peer group for several reasons, including gambling behavior. But there is still some question as to whether peers have a strong influence on early gambling or other risky adolescent behaviors. At this point, all we can say for sure is that family and peer influences as psychosocial variables are correlates or predictors of gambling behavior.

Family Studies

Family studies indicate that pathological gambling may be familial. Adult problem gamblers are three to eight times more likely to report having at least one parent with a history of problem gambling compared with gamblers without problems (Gambino et al., 1993). Also, a similar familial pattern has been observed with college students (Winters et al., 1998) and adolescents (Winters et al., 1993).

Previous research provides mounting evidence that children of alcoholics and of drug abusers are at increased risk for the development of alcohol and drug problems as they progress into adulthood (Goodwin, 1976; Gross and McCaul, 1991). Similar hypotheses about the familial and intergenerational influence of problem gambling on the gambling behavior of offspring have begun to be examined. A sample of predominately white male patients at a Veterans Administration hospital in Boston was asked about their perceptions of addictive behaviors among their parents and grandparents (Gambino et al., 1993). Nearly 25 percent indicated that their parents had problems with gambling, and 10 percent indicated this about their

grandparents. Gambling was the second most prevalent behavior reported after drinking. Those who perceived that their parents had gambling problems were three times more likely to score as probable pathological gamblers on the South Oaks Gambling Screen. Those who also perceived that their grandparents had gambling problems had a 12-fold increased risk.

With a randomized sample of 844 adolescents from four southern California high schools, Jacobs and colleagues found that children who described their parents as pathological gamblers were more likely to report substance use than children who did not identify parents as pathological gamblers (Jacobs et al., 1989). They were also more likely to be overeaters, to be moderate-to-heavy gamblers, and to report resultant gambling problems. However, results such as these may suffer from differential recall bias--that is, people who have had gambling problems are more likely to attribute their gambling behavior to family involvement in gambling and related problems.

Biology-Based Studies

Pathological gambling, classified by the American Psychiatric Association as a disorder of impulse control, has been found to have many similarities to such addictive disorders as alcoholism and drug dependence (Moran, 1970; Lesieur, 1984; Miller, 1980; Wray and Dickerson, 1981; Levinson et al., 1983; Rosenthal and Lesieur, 1992). Similarities include an aroused euphoric state comparable to the high derived from cocaine or other drugs, the presence of craving, the development of tolerance (increasingly larger bets or greater risks are needed to satisfy the gambler, or the same bet or win has less effect than before), and the experience of withdrawal-like symptoms when not betting or gambling (Comings et al., 1996). These similarities have caused researchers in search of the origins of pathological gambling to apply relatively new and sophisticated technologies used in other health research, including twin studies, genetics, brain imaging, and other biology-based strategies. Although only a few studies of pathological gambling involve these technologies, several promising avenues of investigation are emerging.

Genetic Studies

Eisen and colleagues (1997) investigated gambling involvement among 3,359 twin pairs using DSM-III-R criteria, assessed via phone interview. Their original evaluation found that inherited factors explained between 35 and 54 percent of the liability for five individual symptoms of pathological gambling behavior. In addition, familial or genetic factors explained 56 percent of the report of three or more symptoms of pathological gambling, and 62 percent of the diagnosis of pathological gambling (four or more symptoms). This study presented novel evidence that genetic factors have an influence on symptoms of pathological gambling and the development of the disorder.

Winters and Rich (in press) found in a much smaller-scale twin study that, among males, a significant and moderate heritability effect was observed for high-action gambling such as casinos, but not for other types of games. These recent study findings are consistent with that of the earlier classic study of identical twins reared apart by Tellegen (1988); it revealed substantial heritability for impulsiveness as measured by his multidimensional personality questionnaire.

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Neurobiological Mechanisms

Data are accumulating at this time on the association between receptor genes and pathological gambling, for example low-platelet monoamine oxidase activity and high urinary and spinal fluid levels of norepinephrine or its metabolite among pathological gamblers. There is recent evidence that pathological gamblers are more likely than others to carry the D2A1 allele (Comings et al., 1996; Comings, 1998), which has also been linked to a spectrum of other addictive and impulsive disorders (Blum et al., 1996). The implications of these findings and their relevance are explored further.

Theoretically, specific human genes can be linked to biochemical reward and reinforcement mechanisms in the brain, which in turn can be associated with impulsive or addictive behaviors. For example, alcoholism, substance abuse, smoking, compulsive overeating, attention-deficit disorder, Tourette's syndrome, and pathological gambling may be linked in the brain by cells and signal molecules that are "hard wired" together to provide pleasure and rewards from certain behaviors. If an imbalance occurs in the chemicals that participate in this reward system, the brain may substitute craving and compulsive behavior for satiation (Blum, 1996). Recently, research has identified an association between the Taq A1 variant of the human dopamine D2 receptor gene (DRD2) and drug addiction, some forms of severe alcoholism, and other impulsive or addictive behaviors (Comings et al., 1996).

Because the impulsive and addictive disorders that are associated with this variant are also related to pathological gambling, research was conducted to determine if a similar relationship might be present with pathological gambling. Based on this premise, genetic research on pathological gambling theorizes that variants in the DRD2 gene, and perhaps other genes, might be associated with biochemical reward and dysfunctioning reinforcement mechanisms that effectively lead pathological gamblers to behave self-destructively.

Dopaminergic dysfunction, one type of biochemical dysfunction affecting reward and reinforcement systems in the brain, has been at the center of recent genetic studies on pathological gambling. These studies provide preliminary molecular evidence suggesting a genetic pathway to pathological gambling that is similar to that for impulse control and addictive disorders. For example, research findings suggest that the D_2 A1 allele gene type is associated with behaviors that cooccur with pathological gambling, including cocaine abuse, suggesting a possible link between dopamine receptor genes and pathological gambling. Candidate genes for association include the dopamine D_2, dopamine D_1, and dopamine D_4 receptor genes (Comings et al., 1996; Comings, 1998; Perez de Castro et al., 1997).

The Comings laboratory independently collected blood DNA samples from 171 white pathological gamblers recruited from inpatient and outpatient treatment programs, Gamblers Anonymous, and attendees from conferences on problem gambling. Researchers also collected self-reports of gambling behaviors and blood specimens from 102 people in the sample (about 60 percent). A correlation was found between the number of symptoms of pathological gambling and the presence of the D_2 A1 allele gene type. The allele gene was present in a larger proportion of the sample that also met the criteria for a substance use disorder.

The scholarly community has criticized this work on several specific grounds: Does the dopamine dysfunction predict initiation into problem gambling, or only into pathological gambling among gamblers? Because the researchers did not assess substance abuse separately from gambling or for any specific substance, it would be difficult to state with any certainty how

substance abuse, in general, is related specifically to the same receptor as pathological gambling. In addition, the investigators may have misclassified respondents by using a self-administered questionnaire, modified from a structured, diagnostic face-to-face interview assessment tool, to determine psychiatric symptoms and disorders.

In other studies, the D_4 receptor gene has also been targeted as a potential marker for pathological gambling, since there is some indication that it might be associated with novelty-seeking in general, which itself is associated with pathological gambling (Benjamin et al., 1995; Novick et al., 1995) and dependence on opiates (Kotler et al., 1997). Although controversial (Malhotra et al., 1996), this finding, like the one on the D_2 A1 allele gene type, suggests a genetic predisposition that affects the dopamine pathway, resulting in a possible association with pathological gambling. However, these genetic findings are similarly associated with a range of other disorders, such as attention-deficit hyperactivity disorder, oppositional defiant disorder, antisocial personality disorder, Tourette's syndrome, and conduct disorder.

It is important to note that serious controversy surrounds the entire knowledge base on the relationship between dopamine receptor genes and addictive behaviors, with some psychiatric researchers doubtful that such an association has been demonstrated (e.g. Gelernter, et al., 1991, 1993a, 1993b; Cook et al., 1992; Freimer et al., 1996). Thus, firm conclusions about the significance of the work on the relationship between receptor genes and pathological gambling cannot be drawn at this time.

For example, the lack of specificity of association between the dopamine genes and pathological gambling is a concern that must be addressed, so that researchers can better understand the nature of this finding. In view of the general difficulties of establishing genetic relationships to rare behaviors, however, it would be premature to rule out the possibility that some complex interactions involving multiple genes and life experiences play a role in pathological gambling.

The serotonergic (5-HT) neurotransmitter system, part of the system that allows impulses to travel within the central nervous system, has been found to be associated with impulsive, compulsive, mood, and other disorders (Branchey et al., 1984; Brown et al., 1982; Comings et al., 1995, 1996). This system has also been implicated in the development and maintenance of alcohol abuse (Krystal et al., 1994) and cocaine abuse (Lee and Meltzer, 1994). These findings have led investigators to evaluate its association with pathological gambling, since these disorders often cooccur with pathological gambling. Moreno and colleagues have reported a blunted prolactin response among a small sample of gamblers, suggestive of serotonin receptor hyposensitivity (Moreno et al., 1991). DeCaria and colleagues found an enhanced prolactin response in pathological gamblers suggestive of serotonin receptor hypersensitivity (DeCaria et al., 1998). Although these findings are contradictory, they both implicate the serotonin system in pathological gambling. More research is warranted to determine the specific mechanisms through which this dysfunction occurs and how it may affect gambling behavior and other conditions that cooccur with pathological gambling.

Other studies that implicate serotonin have measured platelet monoamine oxidase (MAO) levels. Platelet MAO activity, a peripheral marker of 5-HT function, was found to be lower in gamblers compared with nongamblers (Carrasco et al., 1994). In 1996, with a slightly larger sample (27 gamblers and 27 matched controls), Blanco and colleagues found evidence to support the Carrasco finding (Blanco et al., 1996). A similar finding has been reported for sensation-seekers, risk-takers, and depressed persons (Murphy et al., 1997; von Knorring et al., 1984; Ward

et al., 1987; Buchsbaum et al., 1977). However, these studies must be viewed with caution because low-platelet MAO can also be found in smokers, and smoking is highly prevalent among persons with each of these conditions.

It should also be noted that there are studies that have failed to support a central role for serotonin. In several studies, the metabolites 5 HT and 5 HIAA in the cerebral spinal fluid of pathological gamblers were unchanged (Roy et al., 1988, 1989; Bergh et al., 1997). Studies did find, however, evidence of increased noradrenergic activity. The metabolite of noradrenaline, MHPG, was increased in pathological gamblers (Roy et al., 1988, 1989). Bergh et al. (1997) confirmed that finding and reported an increase in the concentration of noradrenaline.

The clinical severity of pathological gambling has been associated with a growth hormone response to a noradrenergic agonist (clonidine) challenge (DeCaria et al., 1998). Specifically, the level of gambling behavior and cravings to gamble were associated with a growth hormone response, implicating a dose-response relationship between gambling problem severity and levels of this biological marker. This finding is of interest because the noradrenergic system has been associated with increased arousal and pathological gambling (Anderson and Brown, 1984; Dickerson et al., 1987).

Early in pathological gambling research, attention focused on plasma endorphin levels among treatment-seeking gamblers (stratified by type of game played) and nongamblers. For example, Blaszczynski and colleagues (1986), in a study of plasma endorphin levels, found that, with one exception, gamblers did not differ from nongamblers on baseline B-endorphin levels (Blaszczynski et al., 1986a, 1986b). Racetrack bettors, compared with poker machine players, had lower baseline levels. Although this finding has not yet spurred additional studies in this area, it highlights a critical need to consider the type of game played in pathological gambling research.

In summary, a great deal has been learned about the neurobiology factors contributing to drug abuse. Particular attention has been paid to the role of the mesolimbic dopamine pathway in mediating the acute reinforcing effects of most and possibly all drugs of abuse. In fact, drug effects may lead to adaptation in the brain's systems after prolonged drug exposure, and this may lead to addiction. Other brain neurotransmitters may be implicated in drug reinforcement mechanisms. The question is whether these same mechanisms are involved in pathological gambling.

Currently evidence is accumulating for the role of biological factors in the etiology of pathological gambling. In order to present convincing evidence of an association between gambling and biological factors, controlled studies are needed that evaluate gambling history (duration and onset) and environmental factors. Diverse populations also need to be studied. Studies with strong research designs will enable investigators to determine the independent contribution of molecular biological, genetic, and social factors in the development of pathological and problem gambling.

Brain-Imaging Studies [3]

In conjunction with epidemiological, biological, and molecular studies of pathological gambling, the field is now beginning to utilize sophisticated imaging techniques to uncover the brain mechanisms underlying pathological gambling. With evidence that gambling and drug

[3] The committee thanks Scott Lukas for his written contributions to this section.

abuse represent similar subsets of addictive behaviors (Jacobs, 1989a; Gupta and Derevensky, 1996), methods for detecting brain changes among substance abusers can be applied to pathological gamblers. In the mid-1980s, Hickey and colleagues (1986) measured changes in mood state in gamblers as they simulated winning at gambling. The resultant euphoria was indistinguishable from that produced by psychoactive stimulants. More recently, Koepp and colleagues demonstrated that brain dopamine levels were elevated while subjects played a video game for money (Koepp et al., 1998). Since nearly all abused drugs have an effect on the dopamine system, these findings may suggest that gambling (or at least winning while gambling) somehow influences the same basic reward circuits of the brain (Goyer and Semple, 1998). Studies that control for lifetime drug abuse are important, however, since drugs may have a permanent effect on brain circuitry (REFERENCES).

Because various stimuli may reinforce and maintain stimulus-seeking behavior, researchers hypothesize that a shared brain mechanism is at work in a variety of activities, including gambling (REFERENCES). However, a problem emerges when scientists attempt to identify and measure this mechanism. Measuring brain functions in stimulus-seeking situations requires a valid method of communicating behaviors and feelings. It is important that the research methods used to collect these data minimize verbal communication so as to increase the likelihood that the behavioral responses of study subjects adequately reflect the activity of the underlying brain mechanism. To this end, drug studies have used joysticks and switch closure devices to collect relevant data (Lukas et al., 1995; Lukas and Mendelson, 1988; Koukkou and Lehmann, 1976; Lukas et al., 1986; McEachern et al., 1988; Volavka et al., 1973). Implementing such laboratory-type settings for pathological gambling research could be both challenging and restrictive. Investigations into the role of the brain in pathological gambling are further complicated by how little is known about the specific mechanisms that underlie brain dysfunction.

In evaluating any brain function measure, it is important to make the distinction between trait and state categories. Most trait theorists conceptualize traits as dimensional and as relatively stable dispositions, but not as fixed characteristics that cannot change over long time periods. State categories refer to conditions at a given point in time. With respect to trait changes, many investigators have documented specific brain wave changes in individuals with chronic schizophrenia (Goldstein et al., 1963, 1965; Sugerman et al., 1964), depression (D'Elia and Perris, 1973; Von Knorring and Goldstein, 1982), neuroticism (Hoffman and Goldstein, 1981), hyperemotionality (Wiet, 1981), and anxiety (Koella, 1981). To some extent, these changes have been used diagnostically, but their utility in this regard (especially for an individual) is questionable. Changes in state have been studied electrophysiologically for quite some time. Recently other brain imaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI) have also been used to quantify brain states.

This technology allows scientists to examine features of the brain heretofore unavailable to them, but it does not solve all of the problems inherent in this type of research. For example, the mercurial nature of human behavior -- its rapidly changing, unpredictable quality--and the difficulty inherent in quantifying various mood states make drawing conclusions difficult. Despite this problem, brain states, such as mental fatigue, menstrual tension, pain, sexual arousal, meditation, and drug-induced intoxication, have been quantified in this way quite successfully (REFERENCES).

Of particular relevance to scientists studying the brain mechanisms that underlie stimulus-seeking behavior are changes occurring immediately *after* a reinforcing stimulus is administered. In drug use, for example, it is useful to think of such pleasurable, drug-induced behaviors as feeling extremely good, high, or even euphoric as existing on a continuum with other drug or nondrug-related behaviors. The fact that individuals can have cravings for various foods (chocolate, candy, sweets) and for a variety of activities (jogging, gambling, sex) suggests that a neurobiological basis for craving may be similar regardless of the item craved.

Regardless of the source of the change in state, measures of brain electrical activity are well suited for the task. For example, the electroencephalogram (EEG) is available for measurement on a continual basis (i.e., the subject is not required to do anything). Thus, the measurements obtained are free of confounding elements that are often associated with techniques that require a response. With the advent of computer and interfacing technology, methods for recording, quantifying, and displaying brain electrical activity have improved dramatically in the last decade. Lukas (1998) suggests the following research strategies to increase knowledge of the biological basis and etiology of pathological gambling:

- Using EEG, PET or MRI technology to characterize the changes in brain function that are associated with: (a) *winning* during a simulated gambling session, (b) *losing* during a simulated gambling session, (c) different types of gambling (e.g., racetrack, casino, lottery), and (d) the presentation of gambling-related cues.

- Comparing and contrasting the above profiles with the direct effects of psychoactive stimulants, such as amphetamines and cocaine.

- Investigating the generalizability of different gambling-related cues to determine if individual differences exist and dictate the degree of craving.

- Examining the effects of changing reinforcers or simulated gambling behavior.

- Exploring the utility of offering alternative reinforcers in exchange for not engaging in gambling behavior.

- Exploring the utility of using cue desensitization techniques to interrupt the classic conditioned responses to an individual's preferred method of gambling.

- Evaluating the extent to which pretreatment with alcohol (a) increases or decreases gambling behavior or (b) modifies the euphoric effects of winning and the dysphoric effects of losing during a gambling session.

PATHOLOGICAL GAMBLING AND OTHER DISORDERS

Comorbidity is the medical term used to describe the cooccurrence of two or more disorders in a single individual. To qualify as comorbid, each suspected disorder is required to demonstrate the characteristic pattern and etiological basis typically present when each disorder is found by itself (el-Guebaly, 1995). Comorbid illnesses may be described as lifetime

comorbid or currently comorbid. Lifetime comorbidity may describe a situation in which the diagnostic criteria for two or more illnesses were met at some time, although not necessarily at the same time during one's lifetime. Simultaneous comorbidity occurs when criteria for two or more illnesses are met at the same time.

The cooccurrence of other disorders with pathological gambling may be one of the most important and influential indicators of the pathways into and out of pathological gambling. This is because common factors found for different disorders may signal shared familial, environmental, or biological vulnerabilities. Elucidating these factors may improve understanding about prevention and treatment of the comorbid conditions studied. The internal medicine profession is farther along in their search for clues about comorbid conditions than are researchers in the field of pathological gambling. For example, it is widely known that hypertension and diabetes cooccur. Interest in the comorbidity of psychiatric disorders has been increasing as the public health consequences of certain disorders begin to be more heavily scrutinized. In addition, information about the cooccurrence of psychiatric disorders improves the field's understanding of the neurophysiology, genetics, and risk factors associated with these disorders. The occurrence of one disorder with another in an epidemiological study can indicate that one disorder causes another, that there is a common underlying risk factor associated with both disorders, or that comorbid disorders are not independent but simply two phenotypes of the same underlying illness. This ultimately increases understanding of the etiology of the disorders and benefits the development and implementation of treatment strategies (Regier et al., 1990).

As Berkson (1946) showed in his classic mathematical application of hospital data, when information on comorbid disorders comes from studies of treated cases, the data may lead to false associations stemming from the increased likelihood that people with multiple disorders seek treatment and have a better chance of being included in studies. Thus, studies of clinical or treated populations must be viewed cautiously, as any findings of the cooccurrence of illness may be a result of this selection inclusion or Berkson's bias (Berkson, 1946). DSM-IV warns against diagnosing certain disorders if some other specific disorders are already present. In Chapter 2 we mentioned a partial exclusion for pathological gambling in cases for which the clinician believes the symptoms were better accounted for by a manic episode.

Historically, exclusion criteria were designed to ensure that, when studying a given disorder, the group to be studied would be homogeneous to allow for specific and significant findings regarding the risk factors under study. Exclusion criteria originated from the European literature of diagnostic hierarchy, which determined that disorders were hierarchically rated, and that the presence of a disorder from the hierarchy would preclude a diagnosis lower on the hierarchy (Boyd et al., 1984). Jaspers (1946) assumed that this hierarchy corresponded to the idea that no more than one illness could be diagnosed in any one person.

Following a change in DSM diagnostic criteria that only one disorder could be diagnosed per patient, the National Institute of Mental Health funded the Epidemiologic Catchment Area (ECA) study, a landmark study of psychiatric disorders (REFERENCES). In this study, nonclinical interviewers interviewed nearly 20,000 randomly selected people in five sites (data on pathological gambling was collected at only one site, St. Louis, MO). The study showed for the first time, in an unbiased sample, that psychiatric illnesses do occur together, confirming what clinicians--some of whom had treated pathological gamblers--had known for years. Hence, in order to understand what therapies might best reduce or ameliorate suffering from a

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psychiatric disorder, it is vital to understand who is at risk for a psychiatric disorder and what the cooccurring illnesses are.

Evaluating studies of conditions that cooccur with pathological gambling requires careful formulation of research questions, such as: Does gambling precede the onset of other disorders? Do gambling symptoms cluster simultaneously with the other disorder or develop progressively? Do certain disorders exacerbate pathological gambling? Is there a pattern of symptom clustering? Is the severity of one disorder related to the other? And is a standard assessment instrument used to collect data for both gambling and the comorbid condition? Very few pathological gambling studies have addressed even one of these questions. Thus, the field is ripe for etiological research, especially on the topics described in the following sections.

Substance Use Disorders

A review of the literature on comorbidity shows that substance use disorders are most commonly associated with progression to problem gambling and subsequent pathological gambling. The evaluation of the literature is especially interesting given the conditional probability related to both disorders. Specifically, substance abuse or dependence cannot develop in an individual who has never used drugs. Similarly, people cannot get into trouble with gambling if they have never gambled. Thus, investigators must clearly define the exposure conditions for people at risk for both drug abuse or dependence and problem or pathological gambling when reporting comorbidity findings. Specifically, investigators should state the rate of drug abuse only among drug users and should report a conditional rate among nongamblers, gamblers without problems, and pathological gamblers. Rarely has this been done.

A review by Crockford and el-Guebaly (1998) found that rates of lifetime substance use disorders among pathological gamblers in both community and clinical samples ranged from 25 to 63 percent. Other studies reported rates of pathological gambling ranging from 9 to 30 percent among substance abusers (Lesieur et al., 1986; McCormick, 1993). Rather than assess substance use disorders (a task that requires an assessment of the consequent problems from drug use), investigators instead have relied only on the use of substances and gambling. Crockford and others have found that heavy alcohol use is highly associated with increased gambling spending and multiple gambling problems (Crockford and el-Guebaly, 1998; Smart and Ferris, 1996; Spunt et al., 1995). Lesieur and Blume (1986) demonstrated that the rate of pathological gambling increased with the number of substances used. The study was important because it attempted to find a typology of gambling by assessing gambling problems among alcohol users only, among drug users without alcohol use, and among multiple substance users.

In a study of 298 individuals seeking cocaine treatment, those who also had gambling problems were twice as likely as those without gambling problems to have more drug overdoses, greater past treatment for alcohol and for drugs, and more drug use in the past month (Steinberg et al., 1992). They were 1.5 times as likely as those without gambling problems to use opiates and solvents. Studies have found that persons admitted to chemical dependence treatment programs are three to six times more likely to be problem gamblers than people from the general population (Lesieur and Heineman, 1988; Lesieur et al., 1986; Steinberg et al., 1992; Lesieur and Rosenthal, 1998). Natural history studies of gambling and substance abuse are rare. Ramirez and colleagues found that substance use predated the onset of gambling problems in their study

addressing the age of onset of these behaviors (Ramirez et al., 1983). The results might have been different if the onset of drug or alcohol problems, rather than use only, had been evaluated.

Given the reported high prevalence rates of alcoholism among American Indians, one concern since passage of the Indian Gaming Regulatory Act of 1988 is the suspected increase in the comorbidity of alcoholism and gambling for this population. In the first study exploring this relationship (Elia and Jacobs, 1993), researchers, using the South Oaks Gambling Screen among a small sample of 85 patients on an alcohol treatment ward of the Ft. Meade Veterans Administration hospital, found that American Indians compared with whites had a higher rate of probable pathological gambling (22 compared with 7.3 percent) and had more problems from gambling (41 compared with 21.3 percent).

Studies of pathological and problem gambling among general population samples are needed to minimize the bias inherently attributable to treatment samples. The St. Louis component of the ECA study showed that, after adjusting for the effects of a number of variables, gambling without problems and problem gambling were associated with substance use, abuse, and dependence (Cunningham-Williams et al., 1998). In another study, a random sample of Texans was interviewed by telephone about both their gambling and substance use behaviors (Feigelman et al., 1998). The study found that persons with both conditions were more likely than individuals with a single disorder to be psychosocially dysfunctional. These results demonstrate a new direction in gambling research: to discover risk-related typologies for a better understanding of who seeks treatment and of how to prevent gambling problems in the first place. Telephone interviews may not be the best way to obtain information about illegal behaviors, such as drug abuse, however, because people are generally reluctant to acknowledge or provide details of crimes they have committed. As telephone technology improves, it may soon offer a confidential medium for collecting sensitive information that is vitally needed to learn more about the disorders that cooccur with pathological and problem gambling.

Mood Disorders

Early clinical case observations found an association between depression and gambling. In general, these case reports were limited by methodological flaws inherent in small case studies of help-seekers (Moran, 1970; Bishay, 1979). However, a review of these studies documents their importance for informing subsequent comorbidity research (Crockford and el-Guebaly, 1998). Pathological gamblers in some studies did report more depression than nongamblers. Depression scales that measure current depressed mood were commonly used. Given that gambling may stem from attempts to relieve or change subjective states (Jacobs, 1988), it is not surprising that negative affect, or the tendency to experience psychological distress and negative mood states, is frequently associated with gambling severity. However, weaknesses in the studies finding an association between depression scores and gambling need to be addressed. These weaknesses include small samples, minority group exclusion (they are mostly whites), gender exclusion (they are mostly male) and Berkson's bias (gamblers entering treatment for pathological gambling) (Moravec and Munley, 1983; Blaszczynski et al., 1989; Blaszczynski and McConaghy, 1989; Lyons, 1985; Ferrioli and Ciminero, 1981; Roy et al. 1988).

Published studies using diagnostic criteria for depression among gamblers are rare compared with studies that use depression scales. However, the data collected in studies using diagnostic criteria, even if not substantial, are important because they correspond to the

diagnostic nomenclature used by clinicians around the world and address criteria that meet a certain threshold of severity. In fact, because there is a perceived similarity between some of the symptoms of pathological gambling and affective disorders, the DSM-III-R states that, during a manic or hypomanic episode, loss of judgment and excessive gambling may follow the onset of the mood disturbance. When manic-like mood changes occur in pathological gamblers, they are generally related to winning streaks, and they are usually followed by depressive episodes because of subsequent losses. Periods of depression tend to increase as the disorder progresses. Although somewhat reasonable, the current understanding of this progression is informed only by anecdotal information and case histories of patients who have entered treatment.

In one of the first studies to distinguish whether a depression or a gambling disorder came first (i.e., whether pathological gambling was a primary or secondary disorder) McCormick et al. (1984) found that 76 percent of gamblers in treatment met the criteria for a major affective disorder. They also found that gambling preceded depression 86 percent of the time, and even the onset of pathological gambling preceded depression. In another study of gamblers both in and out of treatment, the investigators found, using a structured diagnostic interview, that gamblers in treatment, compared with untreated controls, were about three times more likely to meet criteria for major depression (Specker et al., 1996).

Perhaps the only general population study that has examined the relationship between problem gambling and depression was the ECA study described above. Unfortunately, of the five sites that were involved in the ECA study, only in St. Louis did investigators ask questions to assess pathological gambling. The study found that problem gamblers were at least three times as likely to meet criteria for depression, schizophrenia, alcoholism, and antisocial personality disorder than nongamblers (Cunningham-Williams et al., 1998; Cunningham-Williams, 1998). Because the diagnostic instrument used ascertains the age of onset of psychiatric symptoms, the investigators were able to determine that the depression preceded the gambling problems, unlike the Specker et al. study.

Studies have shown no association between problem gambling and depression, perhaps as a result of methodological weaknesses. For example, Thorson et al. (1994) were unable to find an association between scores on a depression scale (Radloff, 1977) and reported gambling behaviors among nonaddicted adults selected from residents living in Douglas County, Nebraska. The prevalence of gambling was low in this sample, even with the broad inclusion of such activities as entering magazine contests and purchasing stocks and bonds with other, more common forms of gambling like lottery and casino betting. The authors did not evaluate the association between gambling frequency and the amount of depression, which further weakened the association.

Studies have also explored the association between bipolar disorder and pathological gambling. For example, McCormick found that 38 percent of Veterans Administration patients hospitalized for gambling were diagnosed with hypomania (McCormick, 1993). Specker and colleagues found no difference between pathological gamblers and controls for bipolar and dysthymia disorders (Specker et al., 1996). One early study of psychiatric disorders, conducted by Winokur and colleagues (1969), found a high prevalence of problem gambling among families of individuals with bipolar disorder. However, with the exception of the last study mentioned, these findings are based on extremely small sample sizes involving men in clinical settings. As such, conclusions pertaining to associations between bipolar disorders and pathological gambling are not possible at this time.

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Suicide

The literature reports a strong association between rates of suicidal thoughts or attempts and pathological gambling. One of the first studies to find this association was Moran's sample of 162 members of Gamblers Anonymous from the United Kingdom, in which 20 percent of subjects reported having attempted suicide and 77 percent had thought of committing suicide (Moran, 1969). Subsequently, other investigators have corroborated this finding (McCormick et al., 1984; Ladouceur et al., 1994). Frank and colleagues (1991) surveyed 162 members of Gamblers Anonymous by mail to gather information on their suicidal history: 34 reported never having had considered suicide, 77 reported suicidal thoughts, and 21 had attempted suicide (30 did not respond). The researchers found that respondents with a history of suicidal thoughts had an earlier age of onset of gambling compared with nonsuicidal gamblers and were more likely to have engaged in illicit behaviors to support their gambling. Kennedy and colleagues (1971) found that patients who attempted suicide reported gambling more money than nonsuicidal patients.

In another study, 58 male patients in an inpatient treatment program for pathological gamblers in Germany were compared with a control group of patients with other addictions. The gamblers were found to be younger, previously convicted of theft, highly indebted, susceptible to other addictive substances, especially alcohol, and in danger of committing suicide (Schwartz and Lindner, 1992). In yet another study, with a sample from the Compulsive Gambling Society of New Zealand, many gamblers who contacted a nationwide information and counseling hot line reported that they considered suicide as a solution to their gambling problems (Sullivan, 1994). In general, the high rate of suicide among these help-seeking gamblers could be attributed to the sample selection process, since a seriously depressed mood (i.e., suicidal thoughts) increases the likelihood of seeking treatment. The association may also be spurious, in that alcohol abuse and other substance abuse, which are highly comorbid disorders in gamblers, are also strongly associated with depression and suicidal thoughts (Vilhjalmsson et al., 1988).

Only two general population surveys have linked reported suicidal thoughts with pathological gambling. One, the St. Louis ECA study (Cunningham-Williams et al., 1998; Cunningham-Williams, 1998) surprisingly found that the association between the two was not statistically significant. A second study, conducted in 1993 in Canada, was modeled after the ECA study. In that study, investigators reported the rate of attempted suicide among the 30 pathological gamblers (out of 7,214 randomly selected residents of Edmonton) to be 13.3 percent. Although no rate for this behavior among gamblers without problems was reported, there is clearly an increased risk among the group of pathological gamblers in this study, especially when these rates are compared with suicide rates--below 4 percent--in general population studies. This is in contrast to the ECA, in which significant difference in suicide rates was found, although the study designs were very similar. Studies using treatment populations tend to agree with the findings of the Edmonton study. No rate for this behavior among gamblers without problems, however, was provided, so there is no way to determine the increased risk among the group of pathological gamblers (Bland et al., 1993). These findings highlight a lack of association that is contrary to findings using help-seeking populations. They also stress the importance of carefully controlled studies to minimize the risk of making conclusions based on unrepresentative samples, such as a conclusion that pathological gambling

leads to suicide. These findings do not suggest that pathological gamblers never think about or attempt suicide. Rather, these data demonstrate that findings from survey samples representative of the general population predictably differ from findings from surveys of treatment populations.

As with other evaluations of comorbid illnesses, there is the question of whether the gambling precedes or is consequent to depression and the suicidal thoughts or attempt. Although treatment samples have been used to address this issue, they constitute a convenience sample. In one study of 50 patients of an inpatient gambling treatment program, a correlation was found between significant depression and pathological gambling (McCormick et al., 1984). However, as expected from a treatment sample, the researchers were unable to reliably answer whether the depression was the result of, or the enabling factor for, the gambling activities. The research did indicate that relapse into gambling behavior for which help had been sought was common and was often accompanied by suicidal thoughts.[4]

In summary, although these above studies were generally analyzed without multivariate techniques, there appears to be a strong association between depression and gambling. It is not possible to tell, however, whether the depressed mood preceded gambling or was a consequence of gambling. And because the general population is underrepresented in nearly all studies of gambling-related suicide, such a connection from an etiological perspective must be viewed with caution.

Personality and Other Psychiatric Disorders

To date, very few studies have linked personality disorders with pathological gambling. Personality type and its dimensions such as neuroticism, aggressiveness, defensiveness, and socialization have been found to be related to pathological gambling, but the studies have generally been conducted with small samples (Malkin and Syme, 1986; McCormick et al., 1987; Specker et al., 1996). Recently however, Blaszczynski and Steel (1998) found that, of 82 gambling treatment seekers, 76 (93 percent) met diagnostic criteria for at least one personality disorder. In addition "multiple overlapping personality disorders per subject [were] more the rule than the exception" (p. 60). "On average, subjects met criteria for 4.6 DSM-III personality disorders" (p. 65). Consequently, the possibility that pathological gambling is a consequence and not independent of other psychiatric problems must be considered (Crockford and el-Guebaly, 1998).

Interest in the association of antisocial personality disorder (ASPD) with pathological gambling is strong, given that both disorders may be impairing to self, family, and society and each is characterized by persistent irresponsible, socially nonconforming, and risk-taking behaviors. Because these disorders are comprised of similar behaviors, there is an assumption that ASPD is comorbid with pathological gambling, although the evidence has come mainly from studies of gamblers in treatment for gambling or for substance abuse. It has also been reported that from 12 to 30 percent of U.S. and Great Britain and Australia prisoners who are assumed to have ASPD are probable pathological gamblers (Lesieur, 1987; Rosenthal and Lorenz, 1992; Templer et al., 1993; Kennedy and Grubin, 1990). In fact, as Lesieur and Klein (1985) reported in a sample of 230 male and 118 female prisoners, 30 percent were probable

[4] It is also possible that the depressed mood is a combination of major depression and dysthymia--what clinicians refer to as a double depression. Someone may begin gambling to alleviate a depressed mood, but later suffer a second, more acute depression as a consequence of the problems caused by gambling.

pathological gamblers, and 13 percent stated that gambling was either partially or wholly to blame for their detention. However, a spurious association between pathological gambling and ASPD may exist because substance use disorders, which are highly prevalent in these populations, are also associated with ASPD. In addition, research shows that, although gambling usually begins early in life, gambling problems generally occur later. Yet ASPD begins relatively early in life with childhood conduct disorder. It is also true that much pathological gambling may also be illegal gambling and as such might be associated with one or more DSM criteria for a diagnosis of ASPD.

Little is known about the association of anxiety disorders and problem gambling. Only two studies of pathological gamblers in treatment have reported an increased prevalence of anxiety among pathological gamblers, yet the numbers are so small that the meaning is questionable: namely, 12.5 percent in 24 cases of pathological gamblers in treatment (Roy et al., 1988) and 28 percent in 25 cases of Gamblers Anonymous members (Crockford and el-Guebaly, 1998).

Evidence is mounting to suggest an increase in attention-deficit hyperactivity disorder (ADHD) among pathological gamblers compared with nonpathological gamblers. In one study, Rugle and Melamed (1993) found that the groups differed on attention measures, with gamblers showing more attention deficits. Subjects had previously been screened to rule out head trauma, drug abuse, and other medical conditions that might contribute to attention problems. The gamblers also reported more childhood behaviors of ADHD than controls. However, as the authors pointed out, a specific diagnosis of ADHD was not assessed. Further evidence for an association between childhood ADHD and later pathological gambling comes from Specker et al. (1995), who found that pathological gamblers compared with controls were more likely to meet criteria for ADHD. These studies, though conducted with small samples and weak because of their potential retrospective bias, cannot be ignored. They indicate a potential association between early attention problems and later pathological gambling and should be replicated in larger, more representative samples. The data also speak to the need for longitudinal studies of young people, to determine the progression from attention problems to later problems, including pathological gambling.

General Population Studies

To the committee's knowledge, only two studies have assessed gambling and other psychiatric disorders among general population samples, and they are important for that reason. Both studies used the same diagnostic instrument. One study, the ECA, found that, of the associations found, that between gambling and ASPD was strongest (Cunningham-Williams et al., 1998). Problem gamblers were over six times more likely to meet criteria for ASPD than nongamblers. The association with alcohol use disorders was also strong and remained even after controlling for race, gender, age, and ASPD. Furthermore, among problem gamblers with alcohol use disorders, gambling problems occurred within two years of the onset of alcoholism in 65 percent of the cases. Although not one of the stronger associations, nicotine dependence was statistically significantly associated with gambling, with an odds ratio of 2 to 1 (meaning that those with nicotine dependence were twice as likely as those without nicotine dependence to be associated with gambling). Very few studies have reported on the noticeable cooccurrence of smoking and gambling (Smart and Ferris, 1996). Findings of the study pertaining to ASPD and

suicidal thoughts have already been discussed. A second study, modeled after the ECA study, was conducted in Edmonton, Canada. Bland and colleagues found that gamblers were over three times more likely than nongamblers to meet criteria for alcohol and drug use disorders, affective disorder, agoraphobia, obsessive-compulsive disorder, and antisocial personality disorder (Bland et al., 1993). However, the associations presented did not control for either demographic or other psychiatric variables.

Thus, a review of the literature finds that only one study, the ECA report (Cunningham-Williams et al., 1998), was conducted with a general population sample in the United States, used diagnostic criteria, and controlled for the effects of other variables. Although this study has recently been published, it was conducted in the early 1980s and used an older version of the DSM criteria. Also, having been conducted only in a single Midwest city, the importance of replicating such a study nationwide cannot be overemphasized.

CONCLUSIONS

More and better research on the etiology of pathological gambling is needed. As the name of the illness suggests, pathological gambling merely describes a clinical picture. Because the available literature on pathological and problem gambling lacks sophisticated studies enabling this level of discrimination, the committee was not able to say whether the risk factors identified had their impact on initiating gambling, progression to problem gambling, or progression from problem to pathological gambling. Moreover, because risk factors for problem and pathological gambling have usually been dichotomized--that is, respondents either have or have not been exposed to a particular risk factor, and because the sample sizes are small--they are limited in their ability to inform public policy.

Although the past studies have limitations, they have provided the field with a foundation and guidepost for further development. It is now evident that the onset of gambling usually begins in the preteen or adolescent years (Custer, 1982; Griffiths, 1990b; Livingston, 1974) with such activities as baseball card flipping, pitching pennies, and shooting marbles. By adolescence there is poker and sports betting, as well as lottery, racetrack, and casino gambling. Although adolescents can gamble and not become problem or pathological gamblers, certain risk factors, including family member and peer influences, are important for this group. Preliminary evidence suggests that the earlier people begin gambling, the more likely they are to experience problems from gambling. This finding seems developmentally plausible and is consistent with the age of onset and severity for other public health problems, such as substance abuse. It is not clear whether an earlier start at gambling alone represents a risk factor for later pathological gambling, or whether other factors that might drive a person to gamble earlier are also related to developing gambling problems. Little detail is available about natural history of pathological gambling, how long it typically lasts, what causes recovery and relapse. Longitudinal studies would be valuable in answering these questions.

On the basis of the available evidence, we can conclude that men are more likely than women to become pathological and problem gamblers. We do not know yet if gender differences affect all stages of developing pathological gambling, gambling frequency, type of gambling involvement, and the chronicity of gambling problems. More research is also needed to identify risk factors for initiation into and progression of problem gambling behavior for minorities with high rates and to disentangle the complex association between race or ethnicity

and socioeconomic status. More and better research is needed on communities in which gambling access and availability are limited, on the role of incentives for increased participation in gambling, and on identifying personal and environmental barriers to gambling. Such research will show the impact of these risk factors on initiation to gambling and the development of pathological gambling.

As yet, no longitudinal data exist on developmental trajectories of gambling behavior that adequately test aging and cohort effect theories of gambling progression or provide analytical models, such as Erikson's stages of development model, applied to gambling behaviors.

Research on cooccurring disorders in the field of psychiatry is evolving. As the studies noted above indicate, comorbidity research as it relates to gambling is in an early stage. Although studies conducted on treated cases point to important research avenues, results in treated populations may not be generalizable to the population at large. Very few studies of comorbidity evaluate disorders or syndromes, and very few control for the effects of other disorders or for sociodemographic variables. Evaluating comorbidity for descriptive purposes has been a useful first step. Now research is needed that addresses the history of the disorder, and that seeks biological etiologies for these changes. Antisocial personality disorder, substance use disorders, and depression seem to be the most prevalent disorders among pathological gamblers. To advance knowledge about comorbid disorders with pathological gambling, and to identify the disorders that are associated with initiation into gambling as well as progression into pathological and problem gambling, future research will need stronger designs and more rigorous methods. Such research can enhance knowledge and further understanding of how to prevent and treat pathological and problem gambling.

The study of pathological gambling, in its brief development, has no institutional base to sponsor research. The fact that the American Psychiatric Association has adopted pathological gambling into its official nomenclature ensures that it will gain attention. In order to move the science forward, there need to be established funding sources that support the development of measurement tools to assess the consequences of each type of gambling activity and that test them in diverse populations, such as among men and women, young and old, rural and urban, and treated and untreated gamblers. Once the psychometric properties of these tools are firmly established, the field can move expeditiously to identify socioenvironmental, genetic, and family risk factors, as well as the neurobiological and molecular mechanisms that figure in the development of pathological gambling.

The committee concludes, from its review and critique of the literature, that the following specific areas are in critical need of immediate research attention:

- Longitudinal research that explores the transition from childhood to adolescence through later adulthood, to determine the natural history of pathological gambling, including initiation, progression, remission, and relapse.

- Research that controls for important sociodemographic variables in the study of risk for initiation into gambling and progression into problem gambling.

- Family and twin studies to determine familial risk factors for pathological gambling.

- Molecular genetic studies searching for genes that affect initiation into gambling and

progression to pathological gambling.

- Brain imaging research to document the changes that occur during gambling situations.

- Studies that use adequate and diverse samples (racial or ethnic minorities, women, homeless, elderly, and teen populations, rural/urban).

- Research among individuals and communities that examine the effect of access and availability on gambling behaviors.

- Studies on comorbid gambling disorders (especially with mood disorders, substance use disorders, and ASPD), including onset, remission, symptom clustering, related severities of disorders, standard assessments for gambling and other disorders, and multivariate analysis controlling for all comorbid conditions.

- Research on risk-taking and other dimensions of impulse control among gamblers—using adequate controls.

- Research that identifies whether certain games may be gateways to subsequent gambling problems, just as previous research indicates there are gateway drugs that precede the use of hard drugs.

- Studies to determine whether factors are risk factors or consequences of gambling. For example, studies of monozygotic twins with different histories of pathological gambling would be extremely useful.

- Research that encompasses multiple techniques obtaining data from the same participant, such as face-to-face interviews, computer-assisted methods, ethnography, and neurobiological and genetic strategies.

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