

RECENT FORENSIC PHARMACOLOGICAL DEVELOPMENTS IN DRUG ABUSE: THE GROWTH AND PROBLEMS OF SPEEDBALLING

Recent trends in stimulant drug abuse patterns indicate a dangerous resurgence of the "speedball" pattern of depressant-stimulant coadministration, with particular clinical and social problems emerging from the increasing potency and availability of component drugs.

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Increasingly, forensic neuropharmacologists are professionally confronted with patients, often criminal defendants, who have engaged in the practice of speedballing and whose drug abuse is directly or indirectly related to their criminal behavior and their forensic involvement. The "speedball" is a drug abuse strategy that combines the taking of a psychostimulant drug with a depressant or opiate drug. The consequences of speedballing on the neurobiology and on the society of the user are particularly devastating and are orders of magnitude greater than that due to the component drugs alone. The "speedball" components have historically varied over time and in their manner of administration, but neuropharmacologically, the similarity of the various methods lies in the fact that the user's brain is chronically influenced by both drugs either simultaneously or sequentially, with unique behavioral pathology emerging from the combination (Brecher, 1972; *Pulse Check*, 1995 & 1996; Lipman & Tolchard, 1990). The speedballing population is neuropharmacologically as heterogeneous as the component drugs abused, but their common high-dose chronic psychostimulant habitus renders them sufficiently similar to be considered as a class apart.

Growing Incidence

Our common neuropharmacological experience in dealing with drug abusing violent criminal offenders is the emerging realization that "speedballing" is growing at an astonishing rate and speedballers are heavily over-represented in the ranks of capital criminal defendants. Statistics compiled by the Office of National Drug Control Policy only indirectly document the fact that over the past several years speedball consumption patterns have been growing. Typical figures from Region III, which includes the Midwest of the United States, for instance,

record 43% of heroin users also abusing cocaine or crack, a 21% increase over 1994 figures, whilst 7% of crack abusers coadminister heroin and an equal number coadminister tranquilizers, a 20% increase in the 1994 figures recorded in Summer 1995 (*Pulse Check*, 1995). Most recent 1996 figures in the same region indicate that 17% of crack or cocaine users coadminister heroin and 17% also consume amphetamines (*Pulse Check*, 1996). Unfortunately, tranquilizer use was not recorded in this region in this year. Thus, although our statistical methods do not directly track the speedball problem, it can be seen to be increasing dramatically. Another recent development this year is the finding that illicit heroin dealers are now also selling cocaine, previously the retail domain of an entirely different population. The practice has been named "double breasting" (*Pulse Check*, 1996) and almost guarantees the growth of the speedball problem.

The emerging consequences of speedball abuse require entirely different strategies in terms of policing, sentencing and treatment from that which we have traditionally brought to bear on forensic drug abuse problems, which have been largely based on some variation of the alcohol abuse pattern. Not only is the degree of dependence greater, but, as will be explained, the speedball user is frequently paranoid, delusional and frankly psychotic and may additionally be suffering a profound withdrawal syndrome when involved in crime or engaged in legal proceedings. Under these conditions she/he is not deterred by social pressures, constraints of laws or threats of incarceration and competency to plead in court may be problematic.

The Psychostimulant Component

From the forensic neuropharmacological point of view, the societal dan-

ger of speedballing lies largely in the psychosis-producing psychostimulant drug component. This is usually cocaine or an amphetamine, and most recently methamphetamine, an old drug recently rediscovered in new and pure forms by the drug abusing population (Smith & Fischer, 1970; *Pulse Check*, 1995). Unlike the depressant or opiate component of the speedball, the psychostimulants have in common the property of inducing a frank schizophrenia-like psychosis when chronically abused at high doses (Janowsky & Risch, 1979; Post, 1976). The severity of the psychosis is both qualitatively and quantitatively related in part to the underlying psychological vulnerabilities of the user (Satel & Edell, 1991) and also to the intensity, frequency and quantity of dosing, the chronicity (the length of time) of use and the physicochemical properties of the drug itself. The more lipid (fat) soluble the drug, the more rapidly it penetrates the brain, and the more intense its effects, the more severe is the psychosis resulting from its abuse.

The rank order of potencies of the psychostimulant speedball components depends also on the route of administration, where the user's subjective measure of the drug's potency mirrors the speed with which the drug is delivered to the brain. Oral amphetamines are least "potent" on this scale, less potent than "snorted" amphetamine (insufflated into the nose) which is less potent than intravenously injected amphetamine. Smoking the psychostimulant is a relatively recent adaptation which produces an absorption profile not much slower (hence not much less subjectively potent) than intravenous injection (DeCresce et al, 1989). Rendering cocaine smokable requires the user to convert it to its free base, a relatively simple and popular procedure where this is known as "crack", usually mixed with the alkali

salts used in its manufacture. It takes its name from the popping and cracking sounds it makes when a flame is applied to it in the smoking pipe, usually made of glass or modified from a car antenna tube. In part, the greater potency of crack cocaine lies not only in the fact that it can be smoked, but because the base is more lipid soluble than the original hydrochloride salt ("powder cocaine"). Unlike the salt, which dissolves in water and can be injected, the free base is not water soluble without reconversion.

Fashions in amphetamine use among speedballers have followed the same trend toward increased potency as seen with cocaine. Methamphetamine, more lipid-soluble than amphetamine itself, is considerably more potent because it reaches the brain faster. Methamphetamine is also known as "crank", a name popularized in the 1960s by the practice of transporting it in the crank cases of motorcycles. Recent developments in smoking technology among methamphetamine abusers have led to the popularity of a smokable form of the drug called "ice" (which although smokable volatile is, however, *not* a free base, unlike crack) with a corresponding increase in absorption rate by the smoking route bettered only by intravenous injection (Cho, 1990).

The Opiate or Depressant Component

In terms of the depressant or opiate component of the speedball, morphine and its agonist relatives (demerol, meperidine, etc.) are less potent than the more lipid soluble heroin. Subcutaneous injection of these drugs ("skin popping" which is less popular nowadays) is more potent and intense in subjective effect than oral ingestion but less potent than intravenous injection. Smoking produces an absorption rate not much lower than intravenous injection. Nasal insufflation ("snorting") is intermediate between popping and smoking and is less intense but more long-lasting than intravenous injection (Cook, 1991). The snorting of heroin is increasing in popularity in our experience, particularly among snorters of cocaine. Not only opiates, but also barbiturates and benzodiazepines are used by speedballers as the depressant component of their combined drug abuse habit. Historically the barbiturates were preferred in the 1950s and '60s (Brecher, 1972), and methaqualone (Quaalude® in the USA and Man-

drax®, which combined the drug with diphenhydramine, in Europe) was popular in the 70's and early 80's. These depressant drugs have given way to the benzodiazepines in recent years, particularly as newer and more potent benzodiazepines have been developed by the pharmaceutical companies and diverted into the illicit market. Thus Valium®, then Halcion®, and now Rohypnol® (flunitrazepam, also known vernacularly as 'Roofies') are coming into common use by psychostimulant abusers, evolving the speedball practice in new pharmacological directions (Pulse Check, 1995) and broadening the definition of speedballing.

Consequences of Combination

Speedballing, particularly using opiates such as heroin and stimulants such as methamphetamine, is more dangerous to the user and society than psychostimulant abuse alone. This is in part because the opiate enhances certain euphoric aspects of the psychostimulant effect and the psychostimulant enhances certain of the opiate euphoric effects and the two drugs tend to mitigate each other's subjectively felt adverse effects (Lipman & Tolchard, 1990). Thus, the speedballer is able to engage in longer sessions of more intense stimulant abuse, with correspondingly greater behavioral psychopathology due to the psychostimulant component.

Speedballing is also more dangerous than psychostimulant abuse alone because, in contrast to the user dependent on psychostimulant drugs alone, the speedballer suffers a combined withdrawal syndrome due to both drugs when deprived of his or her supply. This is particularly catastrophic when one considers that the chronic psychostimulant psychosis does not abate when the user runs out of drugs, but persists for days and sometimes weeks beyond the last dose administered (Graf et al, 1977). The specifics regarding the withdrawal syndrome differ with different drugs, as described below, but we must first describe the chronic psychostimulant psychosis itself.

Psychostimulant Effects

Used acutely, the amphetamines and cocaine induce in the user a constellation of subjective sensations of energy, competence and power brought about by their increasing

intrasynaptic monoamine levels in the brain. The two drugs achieve this by different mechanisms; cocaine blocking a neurotransmitter (dopamine) reuptake carrier (Malison et al, 1995) and amphetamines forcing excessive presynaptic neurotransmitter release (Samanin & Garattini, 1993). The biochemical and subjective effects are remarkably similar overall despite these different molecular mechanisms. The subjective effect, which is described as a "rush", is one of grandiosity and energy. In hypomanic manner, fatigue is banished, as is the food appetite, and the user rides a wave of sympathetic storm, having engaged the biochemical basis of the "fight or flight" response in which blood pressure is also elevated, sometimes dangerously. The user becomes much more aware (*hypervigilant*) of environmental visual and auditory cues, skills and abilities that were most probably incorporated into the fight or flight response in primordial mammalian development and have their origins in the ascending reticular activating system of the medulla.

Acute psychostimulant abuse can engender an acute brain disorder, with confusion, delirium, agitation and hostility (Cohen, 1975). However, this is relatively rare in the criminal forensic sphere where chronic high-dose abuse is the condition largely associated with serious behavioral psychopathology and violent crime resulting from this. It is principally among the ranks of the chronic high-dose psychostimulant abusers that the problematic speedballers are found.

The chronic psychostimulant abuser engages in periods of protracted use known as "runs", re-administering the drug as its subjective effects wear off for days and sometimes weeks without sleep and with little or no food. The different psychostimulants have their different patterns of use and administration frequency as a result of their different half-lives in blood and brain. Cocaine powder is snorted at approximately hourly intervals, or less, whereas the crack user feels the need to smoke another dose after the passage of only minutes (DeCresce, 1989). Cocaine is very rapidly metabolized to benzoylecgonine which may be responsible for vascular toxicity, heart attacks and stroke. As with alcohol and other drugs of abuse, the subjectively felt need for the next dose is driven by a falling blood level rather than an absence of the drug in the blood and

brain. Amphetamines, in contrast to cocaine, have relatively longer half-lives (4 to 8 hours compared with 0.7 to 1.5 hours for cocaine) and their excretion is dependent in part on the acidity of the urine, acid urine promoting excretion. About 30% of a dose of amphetamine is excreted during the first 24 hours. Methamphetamine is about twice as "potent" subjectively as the dextroisomer of amphetamine and it is worth mentioning that the metabolic inactivation process for methamphetamine converts it first into amphetamine, which therefore continues to exert biological effects (DeCresce, 1989). The methamphetamine injector tends to re-inject every two to four hours as the initial euphoria abates, despite the fact that the drug is still present in the body in appreciable quantities at this time, and pathological accumulation may occur. The "rush" produced by intravenous injection of either cocaine or methamphetamine is universally described as exquisite by those who abuse them in this manner. Very commonly, the first time that a user injects is particularly and pleasantly memorable. Stories abound of the user trying to recreate that "first rush" by repeated injection. We have often heard the refrain: "I've been chasing that first rush for years... just can't seem to catch it again though I get close sometimes."

Chronic psychostimulant abuse engenders a psychotic syndrome that mimics (that is, is mimetic of) the psychosis of endogenous schizophrenia in many respects, a similarity first noted by Young and Scoville (1938) and first reviewed by Connel in 1958. However, since this state is actually organic in origin it is more properly described as a *psychotomimetic syndrome*. The symptoms are *progressively* acquired as the psychostimulant run continues over days and weeks (Hurlbut, 1991). Initial symptoms of hypervigilance become more pronounced and anxiety is heightened. Typically the user becomes paranoid. Initially this paranoia may have some basis in reality, since psychostimulant abusers commonly break laws and fear rivals, but as the psychotic syndrome extends to include auditory and visual hallucinations, the subjects persecutory fears come to revolve around these illusory perceptions. Typical visual hallucinations involve images of threatening persons and shadows seen in peripheral visual fields to be hiding behind trees and shrubs, automobiles or the corners of buildings, who vanish when the user

focuses their attention (and their foveal, central, vision) on them. Delusions regarding how these threats vanished so quickly are common.

There is usually no insight into the hallucinations, as a rule. Auditory hallucinations take the form of two or more voices plotting to attack, often heard through a wall, door or window. Criminal psychostimulant psychotics often hallucinate sights and sounds of police officers, their dogs or radios. Formication hallucinosis is common, this being the tactile hallucination that one is crawling with insects or other foreign bodies (*Formica* is Latin for ant) or some variant of this. We have heard sufferers describe imagined sheets of plastic forming under the skin, beetles living in skin lesions, and other variations on this theme. Very typically the hallucination is accompanied by delusions regarding the nature of the foreign body's reality ("*sheets of plastic form because it dissolves in the syringe, I know this because the plunger gets looser and looser*", or "*Fleas attack me because they like cocaine and they know when I'm smoking crack*"). Not uncommonly the user engages in self-injurious mutilating behavior in connection with these tactile delusions and hallucinations, digging at the imagined insects or foreign bodies with blades and needles. The paranoid psychostimulant psychotic also engages in other behaviors that are based upon their paranoid delusions. Not infrequently, they barricade themselves in their house, cover their windows and doors with aluminum foil or other bizarre materials or pile up cushions or furniture to abate their perceived external threats and achieve some subjective degree of security. They quite commonly arm themselves with guns and knives. They frequently project hostility and harmful intent onto others in typical paranoid fashion and may kill in the mistaken belief they are acting *in extremis* in self defense.

The chronic psychostimulant "run" tends to end in a period of "burnout" called a "crash". The user may then sleep for 12, 24, or more hours, awakening ravenously hungry, often with a particular craving for sweet confections. The withdrawal syndrome from which they suffer after the crash is particularly insidious in that it is largely characterized by a depressed mood, which can be extreme. The psychotic symptoms experienced during the run do not abate immediately after withdrawal, indeed they may persist for days and weeks and in some neurobio-

logically vulnerable individuals they may, rarely, become permanent (Gold & Bowers, 1978; Satel & Edell, 1991). It is commonly believed that in these latter cases the organic psychostimulant psychosis has probably activated a latent or pre-schizophrenic process. The chronic psychostimulant abuser awakening from the 'crash' quickly learns that the depressed effect and the emotional misery of the withdrawal syndrome can be reversed by taking more of the psychostimulant, and so begins another "run".

Depressant or Opiate Interaction in Dependence Formation

The speedball style of combined drug abuse permits the psychostimulant abuser to engage in longer psychostimulant runs using more intense dosing schedules than would otherwise be possible. The depressant drug somewhat relieves the abuser's anxiety and partially allays their agitation. In the case of opiate speedballing, the opiate actually enhances the psychostimulant euphoria and by a parallel process the psychostimulant also enhances the opiate euphoria. Combined use thus engenders a complex pharmacological codependence or interdependence, the user becoming addicted not only to the two drugs used, stimulant and depressant, but to their combination. The work of Wise & Bozarth (1984) provides an explanation of how the dependence engendered by these two drug classes, amphetamine and the opiates in particular, is greater than that of its components: both act on different reward systems "wired" into a common reward pathway in the brain. Brain wave and regional brain metabolism studies have shown that the combination of amphetamine and morphine induces a complex metastate that synergizes, or augments, the amphetamine state (Lipman & Tolchard, 1990). Users report a clear appreciation of this subjective interdependence, describing their depressant or opiate use in terms such as: "I use it to get down so I can get more up."

Notwithstanding the ameliorative effect of depressant or opiate drug coadministration on some of the subjectively undesirable effects of psychostimulant abuse, the depressant does not prevent the development of the psychosis. Indeed, by permitting the psychostimulant abuser to engage in longer and longer runs, the coadministered drug permits a more severe psych-

chopathology to develop. In the case of barbiturate and benzodiazepine co-administration, but not with the opiates, there is the added problem from a behavioral point of view that these depressant drugs induce states of disinhibition, greatly increasing the liability that the paranoid psychotic psychostimulant abuser will act out violently.

Combined Tolerance and "Reverse Tolerance"

As the combined drugs are used chronically, tolerance develops to some of the effects of the components and sensitization or reverse-tolerance to others. This is a particularly psychotoxic characteristic of the speedball habitus. Used chronically, the brain undergoes homeostatic organic changes (tolerance) which tend to diminish the sedative, anxiolytic and euphorogenic effects of the opiate or depressant. These effects are mediated by entirely different mechanisms for the two classes of drugs. Tolerance to the psychostimulant euphoria proceeds progressively, and repeated doses give less energy, alertness and euphoria. In parallel with tolerance development to the psychostimulant euphoria, both cocaine and the amphetamines are unusual in that they engender sensitization or "reverse tolerance" to the psychotomimetic effects of chronic use (Post & Kopanda, 1976). The effect is believed to be mechanistically related to limbic system "kindling" and to a persistent reduction of the seizure threshold of these parts of the brain. As a result of this kindling effect, the user retains increased vulnerability to subsequent psychosis once the state has been achieved and maintained. The anti-epileptic effect of the opiates and the barbiturates and benzodiazepines, which is less pronounced for the former than the latter two agents, may have some as-yet unexplored role in the development of psychostimulant kindling in the speedballer. This hypothesis is presently under study in our collaborative laboratory.

The Combined Withdrawal Syndrome

It is at and following the "crash" that one of the major differences is seen between the abuser of solitary psychostimulants and the speedballer: the speedballer suffers a combined withdrawal syndrome due to both drug classes. These syndromes are different for the opiates on the one hand and the barbiturates and the benzodiazepines

on the other. The syndrome resulting from benzodiazepines and barbiturates more closely resemble each other than they do the opiate withdrawal syndrome. After drug discontinuation the depressant or opiate withdrawal syndrome rides on top of, and neurochemically and behaviorally adds to, both the affectively depressing psychostimulant withdrawal syndrome and the ongoing paranoid psychotic state produced by the chronic psychostimulant abuse (Brecher, 1972).

The barbiturate and benzodiazepine withdrawal syndromes involve a pattern of symptomatology not unlike that following alcohol cessation. This is probably because they share with alcohol a facilitatory action at the brain's receptors for gamma amino butyric acid (GABA, an inhibitory neurotransmitter). Anxiety increases to disabling levels and delirium and ultimately seizures may ensue, which may be life-threatening (Stimmel, 1983, at p170).

For entirely different reasons which depend on the brain's endorphinergic systems, the opiate withdrawal syndrome also begins with anxiety and restlessness, sweating, tachypnea (rapid short breaths), runny nose and watering eyes. Beginning after about ten hours, the opiate withdrawal syndrome differs considerably from the barbiturate or benzodiazepine syndrome, however. As the runny nose (rhinorrhea) and watering eyes (lachrymation) become more severe, the heart rate speeds up (tachycardia) and the sufferer experiences a pronounced tremor and suffers 'goose bumps' (pilo-erection), then nausea, vomiting, diarrhea, fever, and elevated blood pressure. The withdrawing opiate user also experiences repetitive diffuse muscle twitches and spasms at this stage, particularly in the large voluntary muscles (known as "kicking", hence the expression "kicking the habit") and feels burning aches and pains in the joints (Stimmel, 1983). The syndrome waxes and wanes in severity for up to ten days but unlike that following barbiturate or benzodiazepine withdrawal, seizures are not usually seen. The opiate aspect of the speedballer's withdrawal syndrome can be quickly aborted with a relatively small dose of almost any opiate agonist drug. Therefore, the drive to drug seeking behavior is very high, both to avoid the withdrawal syndrome or to stop it once it has started. The user is thus trained to drug dependence by both the carrot and the stick:

the carrot of euphoria and the stick of the withdrawal syndrome.

Forensic Implications

The speedballing criminal defendant is a special and extreme case of the chronic psychostimulant abuser population. They are highly likely to enter the forensic arena as either the victim or perpetrator of violent crime. Unlike the majority of other types of intoxicated defendants, the speedballer may be paranoid, psychotic and deluded and this condition may be exerted longer than the residence of drugs in the blood. Indeed, the paranoid psychosis is joined by profound and varied withdrawal syndromes at such times, exacerbating the condition. Offenses in which they are involved often reflect the behavioral expression of the Organic Brain Syndrome (a highly appropriate term, pharmacologically, although it has been dropped from the most recent Diagnostic and Statistical Manual (DSM-IV) used by psychologists and psychiatrists) from which they suffer and these offenses may be quite irrational. Certain unique behaviors such as pathologically repetitive actions, so called "punding" or "stereotypies", may be expressed as a result of the augmented psychostimulant drug effect. These repetitive actions may superficially and wrongly be assumed to be deliberate or volitional. Repetitive stabbing may thus be mistakenly perceived as heinous malice, for instance, rather than the behavioral perseveration that it is. The speedballer is a particular problem for jail personnel following arrest and very often must be treated psychiatrically for emergency control of both psychosis and the particular withdrawal syndrome they are experiencing.

They also frequently suffer from medical complications of their drug abuse and these can be quite severe (reviewed by Karch, 1993). Notably, epileptic-type seizures that result from barbiturate and benzodiazepine withdrawal can be life-threatening and rhabdomyolysis and infarctions, myocardial and cerebral, can result from both cocaine and amphetamine use, requiring careful medical evaluation and differentiation. Cocaine, of course, can cause heart-block, valvular heart disease, vascular disease (including cerebral vasculitis) and seizures. In the case of cocaine-induced vascular accidents, these are now thought to be mediated in part by the psychoactively-inactive metabolites, perhaps explain-

ing why death often occurs after the parent drug has eluted from blood. Additionally, speedballers invariably suffer comorbid nutritional problems which must also be addressed, these resulting from protracted psychostimulant-induced anorexia

Urine drug testing is essential for proper diagnosis since the mixed symptomatology can not always be relied upon to reveal the underlying combination. In the withdrawal state blood analysis may be negative. Sequential hair segmentation analysis (Lipman, 1996) can be used to assess chronicity of use although the turnaround time of such toxicological studies is presently too slow for emergency treatment purposes. From a criminal defense point of view, the speedballing habitus affects issues of intent and culpability which must be addressed both at trial and sentencing. Lastly, most likely as a result of the kindling phenomenon, speedballing subjects seem more likely than most to re-experience psychotic exacerbation on future relapse into stimulant abuse and they, therefore, present particular problems in terms of planning for the trials and consequences of long-term abstinence.

Conclusions

Over the past twenty years we have watched with dismay the growth and problems of psychostimulant drug abuse get progressively worse with the popularization of newer and more potent forms of cocaine and amphetamines along with the introduction of more pharmacologically active ingestion methods. We have observed the affected population get larger over time and, due to market forces, we have seen the relative prices of these drugs plummet and the doses get larger. We have witnessed the population of users' increasing involvement in violent criminal behavior due in large part to the deranging psychotoxic effects of these psychostimulant drugs on the user's brain. When the problem was

beginning to look as though it could not get worse we observed that it has, by the increasingly common adoption of speedball practices that once were relatively rare. The consequences of the many speedball methods of drug interaction are more problematic by orders of magnitude than the use of these psychostimulant drugs alone. The social, medical and psychiatric consequences are more severe, the acute and chronic therapeutic implications are more problematic, and the forensic implications of dealing with subjects suffering Organic Brain Syndromes who very often cannot be considered "sane" at the time of their misbehavior are taxing our legal system.

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The author wishes to thank Merry Miller, M.D., for editorial review and helpful comments in the preparation of this article.