Revisiting the Self-Medication Hypothesis From a Behavioral Perspective

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The self-medication hypothesis suggests that clients use substances as a means to reduce their psychiatric symptoms. However, substance use as a form of self-medication also can be interpreted as exacerbating symptoms. Behavioral principles may provide a useful perspective to understand this apparent contradiction. The authors investigated the relationship of types of substance use with psychiatric symptoms among 220 participants with co-occurring disorders in an acute care psychiatric unit. Participants were assessed for their use of 6 different classes of substances within 3 months of admission. Hierarchical logistic regression analyses found that particular substances were associated with each of the diagnostic categories and that the pattern of associated substances differed by diagnostic category in a way that supported both self-medication and symptom exacerbation hypotheses. Self-medication and symptom exacerbation can be defined and treated in cognitive-behavioral terms. Harm reduction strategies seem to offer great promise in this context.

PSYCHIATRIC CLIENTS seem to abuse substances at a much higher rate than the general population (Regier et al., 1990). Identifying why this population is at high risk would be very important for formulating appropriate therapeutic strategies to treat clients with dual or multiple disorders. Many clinicians have noted that clients with psychiatric disorders often report using substances to reduce or alleviate various symptoms related to their disorders.

Over a decade ago, Khantzian (1985) proposed that psychiatric clients often self-medicate or reduce their symptoms through the use of substances. Khantzian originally predicted that clients with similar disorders (e.g., schizophrenia) would abuse similar types of substances (e.g., opiates or cocaine) as an attempt to control the disorders (Khantzian, 1985). The original hypothesis was subsequently modified to self-medication of specific symptoms (e.g., negative symptoms associated with schizophrenia) rather than the entire disorder (Khantzian, 1990, 1997). The self-medication hypothesis was controversial because it suggested that substance use disorders, which traditionally had been treated as primary to other disorders, may be secondary to psychiatric symptoms.

Khantzian, a dynamically trained psychiatrist, proposed that self-medication may be mediated through unconscious processes; people are attracted to and choose substances that reduce affective discomfort. Alternatively, behaviorally oriented researchers have suggested that self-medication can be understood as a form of negative reinforcement; the likelihood of substance use increases over time if substance use is followed by the omission or reduction of an anticipated aversive event such as noxious symptoms (e.g., Carey & Carey, 1995). Negative reinforcement of psychiatric symptoms has empirical support; anxiolytic drugs and alcohol use may negatively reinforce anxiety (Busto & Sellers, 1991; Carey & Carey, 1995). Many psychiatric clients with anxiety seem to be at high risk for alcohol and anxiolytic abuse because of the potential for negative reinforcement (Carey & Carey, 1995; Chutuape & deWit, 1995; Roy-Byrne & Cowley, 1990; Schmidt et al., 1989).

Interestingly, neuroscientists have discovered that substances of abuse modulate neurotransmitter release and may have analogs within the brain; specific receptor cells for endogenous opioids (e.g., Kreek, 1996), cannabinoids (e.g., Comings et al., 1997), and benzodiazepines (e.g., Marazziti et al., 1996) have been discovered in the brain. Endogenous opioids, cannabinoids, and benzodiazepines seem important for controlling many psychiatric symptoms (Koob & LeMoal, 1997). Many substances of abuse may moderate natural neurochemical processes via these receptor cells; substance abuse to compensate for neurochemical imbalances (self-medication) is plausible. Compensating for such balances may provide rapid negative reinforcement by alleviating symptom discomfort (e.g., stilling voices or numbing depression).

Behavioral "self-medication" would be supported if people with similar psychiatric disorders had patterns of substance use that reduced psychiatric symptoms (e.g., if clients with depressive disorders tended to abuse stimulants). Tests of the self-medication hypothesis have met with mixed results. Some studies have found that clients with certain psychiatric disorders used substances consistent with symptom reduction (e.g., Dixon, Haas, Weiden, Sweeney, & Frances, 1991; Serper et al., 1995) whereas

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other studies found substance use associated with symptom exacerbation (e.g., Brady et al., 1990).

The latter findings have given rise to a competing biological hypothesis (Miller, Eriksen, & Owley, 1994) that suggests that sensitivities to certain substances can cause or exacerbate psychiatric symptoms and that the psychiatric symptoms are postmorbid rather than premorbid to substance abuse. To confirm this hypothesis, researchers would need to demonstrate that substance abuse produces or exacerbates psychiatric symptoms over time rather than reduce or alleviate them. Acute illicit drug use has been associated with neurotoxicity in key regions of the brain; overuse of these substances may increase rather than reduce psychiatric symptoms. For instance, hallucinogens have produced both manic and schizotypal symptoms in some people (Horowitz, 1975).

Substance abuse may cause a neurochemical imbalance in which natural neuronal processes may become debilitated or inhibited. An invasive substance that may reduce psychiatric symptoms in the short term also can induce a more pronounced imbalance in the long term, exacerbating the original symptoms (Nichols, 1983). Research on this so-called rebound effect has emerged from studies concerning analgesic medications. Analgesic medications, which initially control headaches, can cause an increase in pain after the effects of the medication have diminished (e.g., Mathew, 1997). The rebound effect also has been found for anxiety symptoms related to benzodiazepine use (e.g., Vgontzas, Kales, & Bixler, 1995) and for depressive symptoms after cessation of or withdrawal from psychostimulants (Gillin, Pulvirenti, Withers, Golshan, & Koob, 1994). The rebound effect would not preclude preexisting psychiatric symptoms and would account for symptom exacerbation.

Furthermore, the rebound effect is consistent with behavioral principles. Substance use would be perpetuated by an intermittent negative reinforcement schedule. A particular substance may alleviate symptoms upon first use, and intermittently thereafter. Chronic substance use often leads to tolerance (decreased reinforcement) and neurochemical changes (exacerbation of psychiatric symptoms) contributing to intermittent symptom relief. Intermittent reinforcement schedules are extremely powerful and often lead to behavior that is difficult to extinguish.

Various studies have found that some substances may both reduce and exacerbate symptoms. For instance, opioids have an analgesic effect that may reduce emotional pain in the short term but also can exacerbate depression with long-term usage (Dackis & Gold, 1983). Similarly, marijuana may provide symptom relief for clients with mania (Sonne, Brady, & Morton, 1994) but also may exacerbate mania (e.g., Hollister, 1988); clients with schizophrenia report relief of negative symptoms from alcohol but exacerbation of positive symptoms (Noordsy et al., 1991).

Previous studies have compared clients with psychiatric disorders with nonpsychiatric control participants (e.g., Schneier & Siris, 1987, who outline several examples). The present pilot study compared current substance use patterns among similarly diagnosed psychiatric clients with two nonsimilar Axis I psychiatric disorders. This strategy was done to control for quality of life variables common to people having dual disorders, providing for a more homogeneous sample. Specific substances that were abused immediately prior to hospital admission were assessed among clients with depressive disorders, bipolar disorders (manic phase), or schizophrenia. The self-medication hypothesis would be supported if the abused substances would be associated with reduced psychiatric symptoms. On the other hand, the symptom exacerbation model would be supported if clients abused substances that would increase or perpetuate symptoms related to their disorders. A pattern of use that supports short-term amelioration of symptoms while providing for long-term exacerbation of psychiatric symptoms would support the rebound hypothesis, which may have both biological and behavioral correlates.

Another Look at Substance Use by Psychiatric Diagnosis

A sample of 220 participants was drawn from clients consecutively admitted to an acute care psychiatric inpatient facility located in an urban, public hospital over a 2-year period from October, 1994, through September, 1996. Each participant met *DSM-IV* (American Psychiatric Association, 1994) criteria for only one Axis I psychiatric diagnostic category, including depressive disorders (including major depressive episodes with and without psychotic features and dysthymia), bipolar disorders in the manic phase, or schizophrenia, as well as at least one Axis I substance use disorder. Twenty-one participants also met criteria for Axis II disorders. The participants averaged 35.6 years of age, and the majority was white (N = 163; 74%) and male (N = 169; 77%). Participants who met diagnostic criteria for more than one Axis I psychiatric disorder (e.g., depression and anxiety disorders), psychosis not otherwise specified, or substance-induced mood disorders were not included in the sample to avoid potential diagnostic confounds. During a structured interview with one of the investigators (AB), participants were asked about substances used regularly in the last 3 months. The human subjects committee of the authors' institution reviewed and approved the study protocol.

Hierarchical logistic regression analyses were performed to identify whether specific substances were reliably associated with diagnostic categories. As an analogue to a multiple chi-square procedure, logistic regression analyses can predict models that account for significant

variance in the type of substance use within diagnostic categories.

Results

Table 1 illustrates the descriptive data for the diagnostic categories within the sample. Depressive disorders comprised the most common Axis I diagnostic category within the sample, followed by bipolar disorders, and schizophrenia. Abuse of two or more substances was common (N = 148; 67%) with just 73 participants abusing only one substance. Of these 73 participants, 67 were abusing alcohol, 4 marijuana, 1 methamphetamine, and 1 opioids exclusively. The participants abused an average of 2.4 categories of substances at the time of the interview (SD = 1.3; range 1 to 6). Table 2 identifies the number of participants in each of the three diagnostic categories who abused each of the six classes of substances studied. Alcohol was the most frequently abused substance across all categories (82% of all participants), while stimulants and marijuana (50% and 42%, respectively) were also abused frequently. Hallucinogens and benzodiazepines seemed to be abused sparsely by these participants.

The hierarchical logistic regression analyses found that each diagnostic group abused specific substances when compared with the other diagnostic groups (see Table 3). Participants with depressive disorders were much more likely to abuse opioids alone than were participants with bipolar disorders (manic phase) or schizophrenia. On the other hand, participants with bipolar disorders were more likely to meet abuse criteria for marijuana alone than participants diagnosed with other disorders. Significantly less abuse of both opioids and stimulants was found among participants with schizophrenia compared with people diagnosed with other disorders. Interestingly, alcohol was abused significantly more often among participants with schizophrenia than participants with other disorders (r = .15; $p < .03$). However, in the logistic regression equation, alcohol abuse did not hang together with the more powerful opiate and stimulant predictors.

Table 1
Descriptive Data of the Substances Abused by Diagnostic Categories

Diagnostic category	*Number*	*Percentage of sample*
Depressive disorders	112	50.9%
Bipolar disorders	71	32.3%
Schizophrenia	37	16.8%
Substance abused	*Number*	*Percentage of sample*[a]
Alcohol	181	82
Stimulants	111	50[b]
Marijuana	92	42
Opiates	39	18
Hallucinogens	9	4
Benzodiazepines	8	4

[a] Cumulative > 100% because many participants met abuse or dependence criteria for more than one substance.
[b] 93 patients abused cocaine (42%) and 27 abused methamphetamines (12%).

Table 2
Substances Abused by Psychiatric Diagnostic Categories

Type of Substance	Depressive Disorders		Bipolar Disorders		Schizophrenia	
	N	(%)	N	(%)	N	(%)
Alcohol	89	(79)	56	(79)	35	(95)
Marijuana	43	(38)	38	(54)	10	(27)
Stimulants[a]	62	(55)	38	(54)	11	(30)
Opiates	26	(23)	12	(17)	1	(3)
Hallucinogens	3	(3)	6	(9)	0	(0)
Benzodiazepines	5	(4)	3	(4)	0	(0)

[a] Patients in each diagnostic category abused cocaine [depression, N = 54 (48%); bipolar disorders, N = 30 (42%); and schizophrenia, N = 9 (24%)] more often than methamphetamines [N = 12 (11%); N = 13 (18%); and N = 2 (5%), respectively].

Discussion

Multiple substance misuse was common among the participants of the present pilot study. Furthermore, logistic regression analyses identified specific patterns of abuse within each diagnostic category. For example, participants with depressive disorders were more likely to abuse opioids alone than participants with schizophrenia or bipolar disorders. The analgesic qualities of opiate drugs may negatively reinforce depressive symptoms, especially emotional pain. Similarities in neurochemistry and symptoms found in clients with depressive disorders

Table 3
Hierarchical Logistic Regression Analyses of Axis I Abused Substances by Axis I Diagnoses

Axis I Diagnosis	Predictor	χ^2 (df)	Beta	R	Odds Ratio
Depressive disorders	Opioids[a]	4.79 (1,218)	.79	.09	2.21
Bipolar disorders	Marijuana[a]	6.34 (1,218)	.74	.12	2.08
Schizophrenia	Opioids		−2.01	−.09	0.13
	Stimulants[b]	14.24 (2,217)	−.84	−.11	0.43

Note: Beta and R are $p < .05$ with all significant predictors in the equation; χ^2 values are cumulative within each criterion; odds ratio values reflect goodness of fit within regression model. Positive Beta values indicate positive endorsement of the predictor.
[a] Beta and R are $p < .05$ with all significant predictors in the equation.
[b] Beta and R are $p < .01$ with all significant predictors in the equation.

and in participants with chronic pain (von Knorring & Ekselius, 1994) tend to support the possibility of self-medication for analgesic effects. On the other hand, opioid abuse can also cause or exacerbate depressive symptoms (Dackis & Gold, 1983). These results seem to provide modest support for a "rebound" conceptualization of the behavior pattern of use identified among people with schizophrenia in this sample.

Intermittent negative reinforcement could explain why clients report self-medication yet present with worsening conditions.

Participants diagnosed with bipolar disorders abused marijuana alone significantly more than participants with depressive disorders or schizophrenia. Marijuana has self-reported properties of attenuating affective extremes and racing thoughts related to bipolar disorders (Sonne et al., 1994). On the other hand, THC, the psychoactive substance in marijuana, has been associated with exacerbated symptoms through increased disinhibition and hallucinations for clients with bipolar illnesses (Chaudry, Moss, Bashir, & Suliman, 1991; Hollister, 1988; Marken et al., 1992). Again, these findings for participants with bipolar disorders modestly support a rebound conceptualization of the behavior pattern of substance use: Marijuana use may have been negatively reinforced by reducing certain symptoms but also may have increased symptoms for those susceptible to mania.

The findings concerning schizophrenia and substance abuse are muddled. Participants with schizophrenia in this sample concurrently abused opiates and stimulants significantly less often than participants with depressive or bipolar disorders. Alcohol was abused significantly more often, as has been found in previous studies (Schneier & Siris, 1987), but was not as strong of a predictor as was lack of opiate and stimulant abuse.

Taken together, these data do not provide clear, exclusive support for either the self-medication or exacerbation of symptoms hypotheses for depressive disorders, bipolar disorders, or schizophrenia. Alternatively, a bio-behavioral model may offer a synthesis for the self-medication and symptom exacerbation hypotheses and would be consistent with certain findings in the present study. Greater abuse of opioids among participants with depression and more abuse of marijuana among participants with bipolar disorders seem to support a bio-behavioral rebound model of intermittent negative reinforcement (reports of self-medication) occurring concurrently with evidence of symptom exacerbation. This model could explain why many studies have found contradictory findings concerning substance use patterns within diagnoses, as well as why so many clients report using substances to control psychiatric symptoms yet present in therapy with evidence of worsening conditions.

Clinical Considerations

Consider the case of a 26-year-old male participant in the above study who was prescribed mood stabilizers to control his bipolar disorder. He had a long history of noncompliance with taking his lithium carbonate, and complained about the side effects in great detail. His psychiatrists requested abstinence from marijuana while on the medication, but he rarely complied. He often stated that the marijuana took the edge off the side effects; marijuana, in his words, "helps to slow my thoughts down, and weed works better than the lithium."

Another participant in the above study, a 42-year-old woman with a major depressive episode, indicated that heroin "numbs me out so I don't feel the pain of life." This person also had a long history of repeated hospitalizations, with numerous trials on different SSRIs with limited success. Her psychiatrists insisted upon abstinence as a condition to treatment and could not understand when she relapsed before the SSRIs reached therapeutic dose. She stated that "the drugs take too long to work," adding a comment that why would she want to wait 3 weeks for symptom relief from the prescribed medications when she could find instant relief from the heroin.

These are not uncommon cases. Psychiatric medications can be very unpleasant, by most accounts. Furthermore, people with co-occurring psychiatric and substance use disorders may present with a long history of intermittent negative reinforcement that makes compliance with medical requests for abstinence unlikely.

Addressing "Self-Medication" Issues

The evidence concerning whether patterns of self-medication is supported empirically seems mixed, including in our own study. However, the most pertinent clinical issue, as these cases illustrate, is that many clients *believe* that they are self-medicating symptoms and that the substances they are using are effective, at least part of the time, in reducing the symptoms. These beliefs may be founded upon intermittent symptom relief or may represent a placebo effect at work. Assessing self-medication outcome expectancies may be important in therapy. Furthermore, after a trial of psychotropic medications, a client may be ambivalent about the effects of the medicines after experiencing side effects and latency periods for reaching therapeutic doses.

Because of the positive reinforcement (euphoria) and the intermittent negative reinforcement of substance use, it would not be surprising, from a behavioral perspective, that relapse is common. Furthermore, psychotropic medication often provides delayed or little reinforcement and sometimes seems punishing because of

the side effects. Clients also may have cognitive distortions (positive expectancies or irrational beliefs related to intermittent reinforcement) that have to be addressed therapeutically to enhance adherence. In other words, self-medication may have some physiological elements, but cognitive-behavioral interventions may provide the greatest hope for breaking the behavior chain of rebound. Figure 1 attempts to capture the essence of such a model.

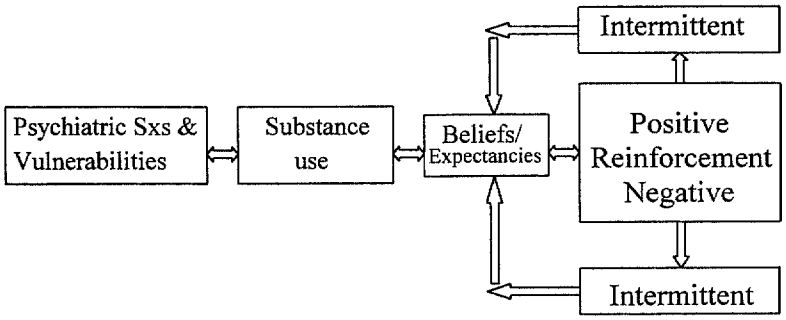

Figure 1. A biobehavioral interpretation of the self-medication hypothesis.

Behavioral Harm Reduction Strategies for "Self-Medicating" Clients

Abstinence may not be a reasonable goal for many clients with co-occurring disorders. However, successive approximations toward abstinence may be more reasonable, so that people reduce substance use slowly as prescribed medicines reach therapeutic dosages. Demanding abstinence as a criterion for entry into therapy seems to promote a revolving-door mentality of treatment. Physicians may unwittingly reinforce noncompliance by readmitting people into therapy. The abstinence criterion may also cause some people not to seek therapy. Establishing a therapeutic alliance with clients who have co-occurring psychiatric and substance use disorders and believe in self-medication of symptoms may be enhanced by compromises concerning continued substance use during therapy.

Relapse prevention strategies may be useful for harm reduction (see Larimer & Marlatt, 1990) among this population. For example, "urge surfing" (Marlatt, 1985) could be adapted to become *discomfort surfing* to cope with side effects of medication or with the latency periods before medications reach therapeutic strength. Meditation practices may help a person "surf" uncomfortable symptoms (e.g., Marlatt & Kristeller, 1999). A functional analysis of the use of specific substances may reveal how the client believes specific substances are controlling symptoms, and self-monitoring may be used to support or dispute those hypotheses. Cognitive therapy may be used to challenge irrational beliefs (Ellis & Velten, 1992) concerning self-medication by pointing out exacerbating effects of the substances or to test hypotheses (Beck, Wright, Newman, & Liese, 1993) that people have concerning the ability of the substances to ameliorate psychiatric symptoms.

Providing the client with access to natural reinforcers in their lives may be a very important role of the therapist. Finding rewards in everyday life apart from substance use is critical. Alternative activities can have the ability to distract and may provide for more structure. Many people with co-occurring disorders have a great deal of unstructured time that may allow for rumination upon unpleasant symptoms. Therapists may wish to teach clients distress tolerance strategies (e.g., Linehan, 1993).

Conclusions

The self-medication model has intuitive appeal: Psychiatric clients often report substance use for the specified goal of controlling or reducing certain symptoms. Self-medication can be understood behaviorally as intermittent negative reinforcement related to psychiatric symptom reduction. Intermittent reinforcement schedules tend to prevent extinction of behavior patterns more than continuous reinforcement (Masters, Burish, Rimm, & Hollon, 1987). Therefore, intermittent reduction or relief of symptoms makes it difficult to break a chain of addictive behaviors. Symptom exacerbation may occur as a result of neurotoxicity related to acute and/or long-term abuse of illicit substances. A biobehavioral rebound model could explain how substances may initially reduce and then later exacerbate symptoms. Intermittent negative reinforcement provides a behavioral explanation for continued usage, in spite of very limited and often sporadic psychiatric symptom relief provided by the substances. Cognitive distortions may perpetuate expectancies that the substances alleviate psychiatric symptoms or that psychotropic medications are unhelpful.

Self-medication involves biological processes but also cognitive and behavioral patterns that can be addressed in therapy. Medical model treatment has not worked well for many people with co-occurring psychiatric and substance use disorders because of unreasonable conditions for treatment. Harm reduction strategies that lower the threshold for entry into therapy, that meet the client where they are at, and that use cognitive-behavioral principles to address cognitive-behavioral problems seem to have promise with this population. Behaviorists are uniquely qualified, in this regard, to provide services for clients with dual or multiple disorders.

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