Attention Deficits in Chronic Methamphetamine Users as a Potential Target for Enhancing Treatment Efficacy

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ABSTRACT

Methamphetamine (MA) is a potent, addictive psychostimulant that has dramatic effects on the central nervous system (CNS). The onset of methamphetamine use has been linked to heightened attention, and chronic methamphetamine use has been associated with deficits in different aspects of attention that can significantly persist into abstinence. Attention deficits in chronic methamphetamine users may be associated with severity of methamphetamine use, craving, relapse, and as a result, poor treatment outcomes. This review summarizes evidence that the continuity of attention deficits, especially during abstinence, should be considered as a potential target during methamphetamine use treatment. Implementing attention rehabilitation techniques during treatment may enhance motivation for treatment in chronic methamphetamine users, and may facilitate treatment adherence, craving control and promote relapse prevention. This issue has important clinical implications for enhancing treatment efficacy and as a result, increasing treatment outcomes.

Introduction

Methamphetamine is an amphetamine derivative and belongs to a class of drugs which is called psychostimulants. There is evidence that chronic methamphetamine use has become prevalent in Iran (Zarghami, 2011) which could lead to widespread harmful health problems, including attention deficits. Short-term methamphetamine use of low-to-medium doses increases productivity, attention, energy and decreases anxiety (Cretzmeyer et al., 2003; Meredith et al., 2005), but psychostimulant drugs such as methamphetamine may be neurotoxic to dopaminergic fronto-striatal brain regions, resulting in significant deficits in selective attention and cognitive control (Nordahl et al., 2003; Quinton & Yamamoto, 2006; Simon et al., 2000).

Models of Attention

Attention is a cognitive process that allows an individual to filter in or filter out environmental events (MacLeod & MacDonald, 2000). In a simple categorization, attention can be divided into two basic categories, including general state of arousal and selective attention. Selective attention is a cognitive function that facili-

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tates the processing of relevant stimuli and inhibits the processing of less relevant stimuli. Selective attention includes voluntary or involuntary attention. Voluntary attention refers to an individual's active searching of stimuli that have individual relevance. Involuntary attention refers to automatic involvement in stimuli when an individual is exposed to unexpected or new situations. This adaptive function of the selective attention mechanism increases the likelihood that most appropriate stimuli will control behavior (Holland & Gallagher, 1999). Sohlberg and Mateer (1987, 1989) proposed a clinical model of attention. It is a model that has proved useful in providing a theoretically grounded method to organize assessment and treatment. This clinical model consists of five components of attention as follows:

1. Focused Attention: This refers to the ability to respond discretely to specific visual, auditory or tactile stimuli. Focused attention is one of the first impaired skills in chronic methamphetamine users and can persist into abstinence.

2. Sustained Attention: This refers to the ability to maintain a consistent behavioral response during continuous and repetitive activity. Sustained attention consists of two subcomponents. One subcomponent refers to vigilance. Disruption of vigilance would be observed in a patient who can only focus on a task or maintain responses for a brief period of time (i.e., seconds to minutes) or who fluctuates in performance over even brief periods (i.e., variable attention or attentional lapses). It also includes mental control or working memory with tasks that involve manipulating information and holding it "in mind". Many chronic methamphetamine users find it difficult to continue performing tasks, even when no distraction exists. For many, exhaustion of their sustained attention leads to fatigue and they may notice that they are making errors or having difficulty with a task.

3. Selective Attention: Selective attention refers to the ability to maintain a behavioral or cognitive set in the face of distracting or competing stimuli. Individuals with deficits at this level are easily drawn off the task by irrelevant stimuli. In other words, selective attention refers to the ability to maintain a cognitive set which requires activation and inhibition of responses dependent upon discrimination of stimuli. An example of problems at this level includes an inability to perform treatment tasks in a stimulating environment. Impaired selective attention would be observed in chronic methamphetamine use and could prolong for months after abstinence.

4. Alternating Attention: Alternating attention refers to the capacity for mental flexibility that allows individuals to shift their focus of attention and move between tasks having different cognitive requirements, thus controlling which information will be selectively processed. Problems at this level are evident in the patient who has difficulty changing treatment tasks once a "set" has been established and who needs extra cueing to pick up and initiate new task requirements. Impaired alternating attention would be observed in chronic methamphetamine users and could be persistent for months after abstinence.

5. Divided Attention: This level involves the ability to respond simultaneously to multiple tasks and demands. Two or more behavioral responses may be required, or two or more kinds of stimuli may need to be monitored. This level of attentional capacity is required whenever multiple simultaneous demands must be managed. Performance under such conditions (e.g., driving a car while listening to the radio) may reflect either continuous and rapid alternating attention or dependence on more unconscious automatic processing for at least one of the tasks. Divided attention can also be impaired in chronic methamphetamine users.

The Importance of Attention Deficits in Chronic MA Users

Several studies have shown that some cognitive functions correlate with clinical or treatment outcome (Leber et al., 1985; Sanchez & Walker, 1982). The majority of studies on methamphetamine users have reported deficits on explicit measures of attention (Nordahl et al., 2003; Barr et al., 2006). Chronic methamphetamine exposure has been associated with an impaired quality of life, and difficulty in carrying out everyday activities. Active methamphetamine users are often involved in sexual activity, partying, shift work, or repetitive tasks requiring simple but focused attention, such as mechanical repairing, house cleaning, or long-distance driving. In a study on the effect of methamphetamine use on everyday functioning in 15 currently abstinent individuals with a history of methamphetamine use and 15 controls, methamphetamine users exhibited significant impairment on the scores related to comprehension, finance, transportation, communication, and medication management compared to controls (Henry et al., 2010). Methamphetamine users are likely to be unemployed (Baberg et al., 1996). Chronic methamphetamine users experience a wide range of interpersonal problems, including poor coping skills, inadequate social support, and disorganized lifestyles (Cretzmeyer et al., 2003;

Halkitis & Shrem, 2006). Some of the effects of methamphetamine use persist for many years into recovery.

The side effects of methamphetamine use are related to duration and intensity of methamphetamine use and could impact short attention span (Rau et al., 2006). Chronic methamphetamine use is also associated with various psychiatric symptoms such as suicidal ideation (Kalechstein et al., 2000) and has been associated with high rates of affective distress in active methamphetamine use (Zweben et al., 2004), acute withdrawal (Newton et al., 2004), and early abstinence (London et al., 2004). Moreover, methamphetamine-associated cognitive deficits and affective distress have been associated with cognitive complaints and self-reported dependence in instrumental activities of daily living (Sadek et al., 2007). Persistent attention deficits impact the occupational opportunities and communication skills of the recovered addicts. Some impairments of performance in complex psychomotor tasks, such as risky driving behavior, are observed. Smart and colleagues (1969) reported on rates of accidents involving a variety of groups of substance users, and revealed that the amphetamine users were the most likely to have an increased accident rate over the driving population in general, but Gardini and colleagues (2009) showed that treatment could contribute to decreases in attention deficits. This issue may also play a significant role in enhancing treatment efficacy and better treatment outcomes for chronic methamphetamine users.

Prolonged Attention Deficits during Abstinence

Cognitive impairments have been reported in chronic methamphetamine users (Rippeth et al., 2004), and are correlated with duration, frequency of use and amount of methamphetamine used. Some studies show that using psychostimulant drugs, such as methamphetamine, could result in significant deficits in attention and cognition (Ernst et al., 2000; Hekmat et al., 2011; Ekhtiari et al., 2010) even during the first weeks of abstinence (London et al., 2005). Some of the neurotoxic effects of methamphetamine are persistent, as the effects are observed during abstinence (Volkow et al., 2001; Chang et al., 2005). Although numerous studies have revealed cognitive deficits in methamphetamine users, few have examined the role of abstinence on cognitive processes (Simon et al., 2004). However, cognitive deficits have been reported in individuals actively using methamphetamine, as well as during abstinence. Research on attention in humans shows that dopamine is involved in attention processing, especially selective attention (Clark et al., 1987), which can remain impaired during abstinence and is associated with attention deficits.

Efforts to prevent methamphetamine use during abstinence could increase attention deficits, hence intensifying methamphetamine users' urge to relapse. This issue may contribute to methamphetamine users' preoccupation with methamphetamine use and their lack of confidence in their ability to manage their daily lives and achieving success in treatment. The early stages of abstinence from methamphetamine use is an important period, because it is the time during which methamphetamine users experience deprivation from methamphetamine use and this can lead to psychological craving and problems in sustaining attention. In addition, the first weeks of abstinence from methamphetamine use is an important period for establishing engagement in treatment, and thus achieving good treatment outcomes (Brecht et al., 2000). However, during the first weeks of abstinence, methamphetamine users display functional and structural changes in specific brain regions that are associated with attention deficits (London et al., 2005). Such impairments can last up to one month (Berman et al., 2007), but Nordahl and colleagues (2005) reported neuronal recovery with prolonged abstinence from methamphetamine use and this was positively correlated with duration of methamphetamine abstinence. Some studies of the brain using magnetic resonance imaging show that white matter, parietal cortical and basal ganglia volumes were larger during early abstinence (<4 months) from methamphetamine use (Thompson et al., 2004; Jernigan et al., 2005), but relatively normal volumes in those with longer abstinence (>20 months) were observed. Simon and colleagues (2000) showed that active methamphetamine users performed poorer than control subjects on tests that evaluated attention.

Marked impairment in the neurocognitive functioning of methamphetamine users persists into abstinence, and becomes worse initially. Other research has established that during early abstinence, methamphetamine users perform worse than controls on measures of attention and psychomotor speed, as well as on fluency-based measures of executive function such as set shifting and inhibition (Kalechstein, et al., 2003). After two months of abstinence, methamphetamine-dependent patients were found to consistently demonstrate errors in selective attention and priming (Salo et al., 2002). In a study of 38 methamphetamine users who recently initiated abstinence, 27 methamphetamine users who had initiated abstinence more than one year prior to study

and 33 healthy controls; the recently abstinent methamphetamine users exhibited greater reaction time (RT) interference compared to both the control group and the long-term abstinent methamphetamine users, while RT interference correlated positively with duration of drug use and drug abstinence (Salo et al., 2009). Simon and colleagues (2010) assessed neuropsychological functioning of individuals during abstinence from methamphetamine use for cognitive change over the first month of abstinence. They compared 27 methamphetamine users during abstinence from methamphetamine use with 28 healthy subjects regarding their attention and processing speed. A sub-sample of 18 methamphetamine users who maintained abstinence for one month, as well as a sub-sample of 21 comparison subjects were retested. In the first assessment, the methamphetamine users showed significantly worse performance than the comparison group on a test of processing speed; they also performed worse than the control group on a global battery composite score. After a month of abstinence, methamphetamine users demonstrated slightly more cognitive improvement than healthy controls on the entire cognitive battery, but this difference was not statistically significant. Researchers in this study found that methamphetamine users did not show significant cognitive gains in the first month of abstinence (Simon et al., 2010).

Assessment of Attention Deficits in Chronic MA Users

Attention deficits of chronic methamphetamine users who attend treatment could be evaluated as part of a larger cognitive or neuropsychological assessment in a therapeutic setting. Evaluation needs to continue throughout the treatment process. There are a large number of standardized tests which can be used to evaluate attention deficits in chronic methamphetamine users. Clinicians can apply a variety of "span" tasks, continuous performance tasks, measures of processing speech and efficiency (e.g., Digit-Symbol subtest), and tasks involving more complex mental control and working memory (e.g., Brief Test of Attention). Multiple measures of attention are required to provide information about the nature and degree of deficits in different domains of attention according to standardized measures, although such measures do not necessarily predict how well a client will function on real-world activities (Sbordone & Long, 1996; Kinsella, 1998). The use of standardized tests with administration of attention-oriented rating scales, structured observations, and an interview in identifying attention deficits and prioritizing treatment options can be useful for this group of substance users. There are a number of rating scales and questionnaires that can help organize clinicians' observations and questions about attention deficits in chronic methamphetamine users such as the Attention Questionnaire (AQ) (Sohlberg et al., 1994) but assessment of attention deficits in chronic methamphetamine users is not limited to cognitive assessment. It can also be assessed in therapeutic settings by reviewing patients' medical details, psychiatric comorbidities and social problems in therapeutic files of chronic methamphetamine users. For example, long hours of insomnia which could result in lack of attention, hallucination which could be associated with insomnia, common psycho-behavioral problems such as history of comorbid disorders including attention deficit hyperactivity disorder (ADHD) can be used as relevant clues for diagnosing attention deficits. ADHD can persist into adulthood, mostly with a symptom profile of inattention and distractibility (Faraone et al., 2000), and it is a risk factor for drug use (Wilens et al., 1995). Moreover, pharmacologic treatments for ADHD (e.g., methylphenidate) target dopaminergic systems, and, similar to MA, operate by preventing reuptake of dopamine and norepinephrine (Pliszka, 2007). This issue has led some researchers to propose that individuals with ADHD may experience more positive effects from initial MA use, leading to repeated use and dependence (Jaffe et al., 2005). Some studies show that ADHD in adulthood is related to a dopamine deficiency in the midbrain which is responsible for attention and regulation of motor activity (Kim et al., 2002).

Observation of behavior is another valuable assessment tool. The clinician should take note of the responses of the client's natural distractions and tracking verbal interactions. Structured interviews can provide additional information and can suggest the most important contexts for observation in the assessment stage. Information from structured interviews can also be very helpful in charting progress in treatment for chronic methamphetamine users. It should be noted that attention is a cognitive ability that can be easily affected by emotional variables such as depression and anxiety and physical variables, such as fatigue, which are frequently observed in chronic methamphetamine users. In order to fully address attention deficits in a chronic methamphetamine user, the clinician will need to consider potentially important physical, emotional, behavioral and social variables.

Rehabilitation of Attention Deficits in Chronic MA Users

The cognitive deficits decrease users' cognitive sharpness (Stormark et al., 2000) which in turn, lowers their ability to remain in treatment and this issue could predict later dropout. Attention deficits especially during abstinence could contribute to craving or relapse if they have not been treated, but study on treatment options for this problem is notably scarce. Partial recovery of cognitive function following both short (i.e., two weeks; Chou et al., 2007) and long (i.e., more than six months; Wang et al., 2004) periods of abstinence can occur. This evidence points to the need for interventions that directly target the attention deficits to precipitate recovery. Chronic methamphetamine users may benefit from interventions that help decrease their attention deficits, and thus positively influence their recovery procedure. Neurogenesis can occur during abstinence and precipitate decreasing attention deficits but neurogenesis will only regenerate when they are repeatedly stimulated to do so. This long-term period of neural repair requires a coherent, comprehensive approach of counseling, psychiatric care, nutrition, emotional support and engagement in cognitive tasks which can increase, direct and sustain attention. Successful treatment of chronic methamphetamine users must be associated with reductions in problematic attention deficits. Other treatment interventions for attention deficits during abstinence are necessary and should address both cognitive and motivational mechanisms underlying attention deficits. Attention rehabilitation training could be a valuable treatment.

Therapeutic approaches that include pharmacological as well as behavioral interventions could also benefit the patients. For example, Ritalin (methylphenidate) can be prescribed for those methamphetamine patients who suffer from adult ADHD because Ritalin increases dopamine release and enhances focus and attention especially in activities such as driving (Jerome & Segal, 2001). In general, five approaches to address difficulties in attention have been proposed which could also be used for rehabilitating attention deficits in chronic methamphetamine users. In order to rehabilitate attention deficits, most often a clinician can implement some combination of these approaches either simultaneously or at different times in the treatment process (Sohlberg & Mateer, 1989). These include environmental modifications and supports, attention process training, self-management strategies, use of external aids, and psychosocial support respectively. Implementing environmental modifications and supports could be effective in managing attention deficits of chronic methamphetamine users. Careful assessment of the environment could be part of any cognitive management plan of chronic methamphetamine users. The procedures of implementing environmental modifications and support include reducing distraction and facilitating organization. The outcome of this approach includes improving content for cognitive processing. Establishing environmental supports requires planning and monitoring. Careful assessment of the context, having a plan for measuring success or lack of success, ensuring the methamphetamine user and others involved in the modification, and allowing them to get familiar with using the supports is important for the effectiveness of this intervention. Given the individual nature of the strategies and environmental supports, the research literature is limited to case studies as evidence (Mateer, 1997; Sohlberg, 2000). Attention Process Training refers to providing opportunities for stimulating a particular aspect of attention which can be effective in improving attention deficits. The procedures of implementing attention process training include reducing cognitive exercises, and generalization training. The outcome of this approach includes improved processing efficiency, and increased self-awareness. Treatment involves having clients engage in a series of repetitive drills or exercises that are designed to provide opportunities for practicing tasks with increasingly greater attentional demands. Studies show that repeated activation and stimulation of attentional systems facilitate changes in cognitive capacity (Park et al., 1999; Sohlberg & Mateer, 1987).

There are a number of attention training packages available for use. One example is the Attention Process Training program (APT) (Sohlberg & Mateer, 1987; Sohlberg et al., 1994). It is a widely used cognitive rehabilitation program designed to rehabilitate attention deficits in individuals with brain injury, but it may be partly used for rehabilitating attention deficits in chronic methamphetamine users. The APT materials consist of a group of tasks that exercise different aspects of attention impaired after brain injury, including sustained, selective, alternating, and divided attentions respectively. Measurement of improvement at the level of everyday functioning is the most significant indicator of success or failure of attention training. Self-management strategies could also be used in conjunction with attention process training for chronic methamphetamine users. Self-management strategies include reducing, orienting, pacing, and key ideas respectively. They involve self-instructional routines that help a client focus attention on a task. The outcome of this approach includes increased sense of self-control, and personal empowerment. Ori-

enting procedures may be helpful in reducing sustaining attention or screening out distractions. These procedures encourage an individual to consciously monitor his/her activities, thereby avoiding attentional lapses. Teaching clients to ask themselves orienting questions at a specified time is an example of implementing orienting procedures. Clients with attention deficits often experience difficulty with fatigue or maintaining concentration over an extended period of time, therefore teaching pacing strategies may be helpful. Pacing allows clients to continue for a longer period of time but it must be individually applied. Involving the client and relevant key persons in the design and piloting of a pacing strategy will be important in ensuring that it will be utilized. Another attention problem that interferes with day-to-day functioning in chronic methamphetamine users is difficulty in switching between tasks. A common complaint is that individuals cannot resume an activity if they are interrupted or must temporarily divert their attention. To manage this difficulty, individuals can learn to quickly jot key questions or ideas that come to mind that need to be addressed later on. This allows them to continue with a particular task. There are a number of external devices and aids that assist individuals in tracking information and initiating planned activities such as written calendar systems with day planners, task-specific devices and checklists. Although these techniques have been basically used for clients with brain injury, they may also be effective in rehabilitating attention deficits in chronic methamphetamine users.

The importance of psychosocial support for managing attention deficits cannot be underestimated. Effective management of attention deficits in chronic methamphetamine users requires a clinician to be skilled at providing psychosocial support as well as neurocognitive intervention. Decreased attention ability may be the result of an interaction between neurological impairment and psychosocial factors. It is important to acknowledge the interaction between neurological dysfunction and psycho-emotional difficulties when designing a rehabilitation program for rehabilitating attention deficits in chronic methamphetamine users. Helping clients track the contexts where their attention processes break down, as well as situations where their attention is functioning well, often leads to a perception that attention is improving. Studies show that people with brain injury may inadvertently do things to improve their functioning due to increased self-monitoring. Alternatively, these people may feel more in control when they are assisted to pay attention to their own functioning during their day-to-day life (Sohlberg et al., 1998). This issue could also be the same for chronic methamphetamine users. No single technique of rehabilitation is universally accepted for treating attention deficits in chronic methamphetamine users but long-term treatment interventions are needed for many months, even years, after completion of the treatment program.

Lack of Clinical Data for Cognitive Rehabilitation

Applying attention rehabilitation techniques may be associated with improved functioning on focused attention, sustained attention, selective attention, alternating attention, and divided attention on a day-to-day basis as well as greater improvement on neuropsychological test performance, and engagement of chronic methamphetamine patients in methamphetamine use treatment. Although there are as yet little data with regard to the effectiveness of these approaches in chronic methamphetamine users with attention deficits, there is a growing literature suggesting they may be effective in people diagnosed with brain injury and other disorders. For example, in their study on brain-damaged patients, Sturm and colleagues (1993) showed the effectiveness of attention training in increasing attention, reporting improved performance on neuropsychological tests specific to the type of attention that was essentially trained. Further, in a series of studies on non focal brain injury, and post-concussive syndrome, Mateer and colleagues (1988, 1992) reported improvement following attention training not only on measures of attention, memory, and learning, but on levels of independent living and return to work. Sivak and colleagues (1984) reported improved driving performance following perceptual skills and attention training in a group of individuals with brain damage.

Clinicians can apply these approaches to rehabilitate attention deficits in chronic methamphetamine users but the effectiveness of such approaches in decreasing attention deficits should be extensively evaluated. It should be noted that measurement of improvement at the level of everyday functioning is the most important indicator of success or failure of attention rehabilitation techniques. Some studies show experience-dependent recovery processes due to changes in synaptic connectivity (Tallal et al., 1996). It may be also the same for chronic methamphetamine users. Clinicians can apply neuroimaging studies which elucidate experience-dependent changes in neural functioning for detecting changes that the implementation of attention rehabilitation techniques could bring to chronic methamphetamine users.

Discussion

Studies implicate chronic methamphetamine use in metabolic and neurotransmitter abnormalities, structural brain alterations, and deficits in everyday functioning, which are attributed to neurotoxic effects of methamphetamine use on the central nervous system. These alterations may also contribute to significant neuropsychological impairments including attention deficits. This issue corresponds with clinical observations that methamphetamine users are distractible and have difficulty in maintaining attention (Nordahl et al., 2003). This issue is also highlighted by reduced attention ability, decreased capacity for information processing and reduced ability to manipulate new information in chronic methamphetamine users. Methamphetamine use causes damage to attention. Therefore, users who become abstinent from methamphetamine use may face irreversible neurological deficits resulting in long-term difficulties with attention and as a result, poor treatment outcomes. Attention deficits result from the affected brain areas (Salo et al., 2002) and include deficiencies in focusing, sustaining, selecting, alternating and dividing attention. Attention deficits have also been shown to be proportional to the amount, frequency, and duration of methamphetamine use. Chronic methamphetamine use is associated with elevated cognitive complaints and self-reported dependence in IADL (e.g., preparing meals, managing money). A study showed that IADL impairments were strongly associated with depressive symptoms, whereas cognitive complaints were significantly related to both depression and objective neuropsychological impairment (Sadek et al., 2007) in chronic methamphetamine users.

The reason for the current focus on attention deficits is that these deficits fuel the motivation to use methamphetamine and can eventuate actual use of it and as a result, poor treatment outcomes. Moreover, attention deficits are undesirable for abstainers because of mood disturbances and interference with thought processes and daily activities (Bradley et al., 2001). The prolonged effects of methamphetamine use on attention suggest that methamphetamine use treatment must be partly allocated to rehabilitate attention deficits. This issue could act as an important facilitating factor in increasing patients' engagement in treatment and enhancing treatment efficacy. Long-term treatment interventions including pharmacological, behavioral, cognitive, and nutritional interventions are necessary to lower the neurotoxic effects of methamphetamine use on attention deficits. It should be noted that certain treatment models including the Matrix Model have been mainly used to treat chronic methamphetamine users (Anglin & Rawson, 2000) and these treatment models cannot be solely successful while attention rehabilitation techniques are not simultaneously applied. Treatment of attention deficits is a long-term process and it currently lacks extensive research. Nevertheless, similar attention training programs have been designed and used for other patients including patients with brain injury (Ben-Yishay et al., 1987) and could be modified and used for chronic methamphetamine users. To determine whether an intervention has been successful, we suggest embracing therapies that produce and build upon a so-called placebo effect and thereby empower chronic methamphetamine users to understand and modify their circumstances. The understanding of how attention deficits recover as a function of prolonged methamphetamine abstinence has important clinical and treatment implications. If improvement in attention occurs across prolonged periods of abstinence, this finding would be clinically important. These cognitive improvements can then be applied in methamphetamine use treatment programs and can be utilized as predictors of treatment effectiveness in difficult patients (Streeter et al., 2008). As a result, knowledge regarding recovery of attention deficits could help to better apply those techniques that can be used to rehabilitate attention deficits. Such information could help to optimize the timing of cognitively demanding interventions. Attempts to design novel rehabilitation techniques to manage attention may contribute to emerging new treatment options to improve attention deficits in chronic methamphetamine users. There are as yet little data with regard to the effectiveness of these approaches in rehabilitating attention deficits of chronic methamphetamine users and further investigation of the evaluation of such techniques in chronic methamphetamine users with a wide variety of attention deficits is suggested.

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