

September 2014

Treating Cocaine Dependency with Psychopharmacotherapy and Behavioral Therapy

Robyn Liebman

Follow this and additional works at: <http://digitalcommons.chapman.edu/e-Research>



Part of the [Chemicals and Drugs Commons](#), and the [Pharmacology Commons](#)

Recommended Citation

Liebman, Robyn (2014) "Treating Cocaine Dependency with Psychopharmacotherapy and Behavioral Therapy," *e-Research: A Journal of Undergraduate Work*: Vol. 1: No. 2, Article 8.

Available at: <http://digitalcommons.chapman.edu/e-Research/vol1/iss2/8>

This Article is brought to you for free and open access by Chapman University Digital Commons. It has been accepted for inclusion in e-Research: A Journal of Undergraduate Work by an authorized administrator of Chapman University Digital Commons. For more information, please contact laughtin@chapman.edu.

e-Research: A Journal of Undergraduate Work, Vol 1, No 2 (2010)[HOME](#) [ABOUT](#) [USER HOME](#) [SEARCH](#) [CURRENT](#) [ARCHIVES](#)

[Home](#) > [Vol 1, No 2 \(2010\)](#) > [Liebman](#)

Treating Cocaine Dependency with Psychopharmacotherapy and Behavioral Therapy**Robyn Liebman****Abstract**

Cocaine is an addictive drug that affects more than 14 million people globally, according to the United Nations. This paper is a conceptual meta-analysis of numerous studies that tested the effects of psychopharmacological therapy along with behavioral therapy in the treatment of cocaine addiction. It is hypothesized that cocaine dependent individuals treated with a combination of psychopharmacological and behavioral therapies will be less likely to use cocaine. Measurements of cocaine use throughout the experiments were generally assessed by urine screenings. Results indicate that there is more evidence that a combination of psychopharmacological and behavioral therapies will reduce cocaine use. There are no indications that any specific type of psychopharmacology is more effective than others. This literature review suggests that, while there is no specific category of medication that is most effective in the treatment of cocaine addiction, more studies should be conducted, as it is a promising option that could be utilized along with behavioral therapy.

Keywords: Cocaine Dependence, Behavioral Therapy, Psychopharmacotherapy, Treatment**Introduction**

Cocaine is a highly addictive stimulant drug that affects the central nervous system. It is the most potent stimulant that is derived from natural origin. Cocaine was introduced in the 1880's as a local anesthetic used for blood vessel constriction to limit bleeding in eye, nose, and throat surgeries (Drug Enforcement Administration). Sigmund Freud, among other doctors, recommended cocaine as a treatment for many ailments such as; upset stomachs, tuberculosis, depression, and hay fever (Courtwright, 1991). Cocaine was also used to help treat opiate addictions, before it was discovered to be an addictive substance itself (Musto, 1989). Due to the substantial use of cocaine to treat ailments in the late 19th century, a wave of dependency and addiction affected men, women and children.

A. Background & History

Robyn Liebman

.....
The use of cocaine in America has undergone three stages. First cocaine was introduced in the 1880's as a treatment option for ailments, and as it was shown to be effective, it gained acceptance and popularity as it entered its middle stage, only to be shortly recognized and feared as an illicit drug and treated as an illegal substance, which was its final stage (Musto, 1989). Cocaine has become the second most widely used recreational drug in America (Drug Enforcement Administration).

When abused, cocaine creates a euphoric sensation and causes blood pressure, body temperature, and heart rate to rise (Drug Enforcement Administration). The brain experiences an increase of dopamine release in the nucleus accumbens, activating the meso-cortico-limbic system (Karila et al., 2008). The dopamine system is important in motivation, emotion, information processing, as well as a reinforcement mechanism. This is why the drug is extremely addictive. Cocaine manipulates other neurotransmitters, such as glutamate, GABA, endocannabinoid, corticotrophin, and norepinephrine (Karila et al., 2008). Due to the way cocaine affects numerous neurotransmitters, there are various psychopharmacological approaches currently being tested in the treatment of cocaine dependency.

History of Treatment

Most of the time, patients do not experience the effects of the medications until a few weeks after they begin pharmacological treatment. For this reason, it is important to utilize cognitive behavioral therapy along with psychopharmacotherapy in order to begin the recovery process before the medication is effective.

Over the past 30 years, behavioral therapies have been widely studied for use in the treatment of drug and alcohol dependency. There are various types of behavioral therapies that have been researched, and the most effective are Cognitive Behavioral Therapy and Contingency Management (Carroll, 1998). By utilizing behavioral therapy treatment approaches, cocaine dependent individuals have demonstrated improvement (McKay et al., 2010).

a. Behavioral Therapy

Cognitive Behavioral Therapy is considered effective for the treatment of cocaine dependence for various reasons. It is a short-term therapy option that is effective in the treatment of cocaine addiction and it is especially efficacious for those that are severely dependent on the drug (Carroll et al., 2004). This behavioral therapy focuses on the immediate problems that patients are dealing with, and is a structure and goal-oriented approach in treating and coping with these direct issues. It is easily adaptable and flexible to the individual's needs in therapy and controlling dependency behaviors (Carroll & Onken, 2005). In general, those who are dependent on cocaine utilize the drug as a coping mechanism for underlying problems. The skill training of cognitive behavioral therapy teaches individuals to deal with their habits and to be aware of what they are doing in response to their

interpersonal and intrapersonal issues. Cognitive behavioral therapy is highly effective in combination with pharmacotherapy for other issues, for example, depression.

b. Contingency Management

Another type of behavioral therapy, contingency management, has also been effective in the treatment of cocaine dependency. Contingency management is a behavioral therapy that systematically reinforces desired behaviors, and withholds or punishes undesired behaviors (Higgins & Petry, 1999). The most effective type of contingency management to treat drug dependency is a reward-based technique that systematically provides the participant with an incentive, or voucher, that can be cashed in for a monetary value or a prize. The patient receives these vouchers after demonstrating the desired behavior, based on a previously determined criteria and schedule. Both prize and monetary vouchers produce significant patient outcomes, as demonstrated in a study conducted by Olmstead and Petry (2009), and therefore both are utilized in numerous cocaine dependency studies as a behavioral therapy technique. A study conducted by Higgins et al. (2005), found that contingency management was effective in numerous ways; it was well accepted by patients, had high retention within subjects, was effective in achieving initial cocaine abstinence, and was able to retain abstinence in cocaine dependent individuals. Contingency management, although effective on its own, is often combined with cognitive behavioral therapy for the treatment of those who are dependent on cocaine, in order to ensure a successful recovery.

All behavioral therapies have been shown to be effective in treating drug dependence, however, there are currently no psychopharmacological treatments for cocaine dependency. Currently no FDA approved pharmacological treatments for cocaine dependency exists. Those that are dependent on cocaine are often treated for co-existing psychiatric disorders, and this is the only time the psychopharmacotherapies for cocaine substance abuse are usually utilized (Carroll & Onken, 2005). Many cocaine dependent individuals self-medicate concurrent psychiatric issues, and thus if the underlying issue is treated, the cocaine dependency will ease. Therefore the combination of psychopharmacological and behavioral therapy is a promising outlet for the treatment of cocaine dependency.

Prevalence

Substance Abuse and Mental Health Services (2008) estimates that approximately 36.8 million Americans have used cocaine, representing 14.7% of the population. Although statistically cocaine use in the United States has decreased by an estimated 25% since 2006, the National Drug Intelligence Center (2010) attributes this decrease to the increasingly high demand of cocaine in other parts of the world. Cocaine is an outstanding problem among Americans. Although recent studies suggest cocaine use is decreasing slightly, the amount of people who use it is still astronomically high, indicating that a treatment option is necessary to lower the rate and prevalence of cocaine dependency and abuse (National Drug Intelligence Center, 2010).

Robyn Liebman

The history of cocaine indicates what can happen in the future if cocaine dependency and addiction issues are not dealt with. Epidemics such as the widespread addiction among men, women and children in the 19th and early 20th centuries lead to legal and social consequences including crime and gateways to other addictive substances, such as heroin (Courtwright, 1991).

A. Problem

1. Cost

The treatment of cocaine can be very costly. It is estimated that the United States spends over \$414 billion annually on substance abuse disorders, and a large portion of that is dedicated to the treatment of cocaine dependency (Quality Enhancement Research Institute, 2008). Due to the highly addictive nature of this drug, there is a great deal of costs involved with the treatment and rehabilitation to assist and maintain those that are dependent. Although the treatment costs for each individual vary based on time in treatment, needs, and type of therapy, there are various categories that these costs are divided into. Some common categories include treatment personnel, administration and office personnel, space, equipment, transportation, communication services, and insurance, to name a few (National Drug Intelligence Center, 2010). The cost involved in treating those with a cocaine dependency can be steep. Treatment is not the only cost involved with the issue of cocaine use. The transportation and illegal trade of drugs is a huge cost that America pays for every year.

2. Social Complications

The use of illegal drugs, especially cocaine, has many negative social effects. Cocaine can cause permanent physical and emotional damage, which in turn negatively affects family members, coworkers, and friends (National Drug Intelligence Center, 2010). Drug abuse leads to health complications, and sometimes death, which can cause subsequent child abandonment, if that individual had children, and an increase in the number of children placed into foster care.

3. Cocaine Related Crime and Violence

The most common arrest category and population in prisons and jails is criminals that have broken the law pertaining to drug use and abuse. The Bureau of Justice estimates that 53% of the federal prisoners are incarcerated on a drug related offense (National Drug Intelligence Center, 2010). These criminals are then placed into the legal system, monopolizing time, money and resources that are needed for the prosecution of other violent offenders. Drug related crimes are the largest category of arrests made and they account for 12.2% out of 14 million arrests, which has increased over the last 20 years (National Drug Intelligence Center, 2010). Studies have shown that when stimulants are used, human behavior increases in competitiveness, excitability and

volubility (Hoaken & Stewart, 2003). Overall cocaine has negative social effects, health complications, and increased rates crime and aggression.

4. Infectious Diseases

Cocaine use leads to the transmission of infectious diseases. Users who inject cocaine are at risk of contracting HIV and viral hepatitis. Along with these risks cocaine reduces immunity and increases susceptibility to infectious diseases (Friedman, Pross & Klein, 2006). Besides the known health risk of using cocaine, a new epidemic is threatening the population of cocaine users. A pharmaceutical agent called levamisole is appearing in higher quantities in cocaine samples obtained. This drug is typically used in the deworming of livestock, and is harmful to humans causing agranulocytosis, a fatal blood disorder (Drug Enforcement Administration, 2005). Individuals are not always aware of what the cocaine is laced with, and the substances that are mixed with cocaine can be fatal.

C. Purpose and Goal

The purpose and goal of this paper is to assess the effectiveness of pharmacotherapy and behavioral therapy, compared to behavioral therapy only, in the treatment of those who are dependent on cocaine. Various classes of psychopharmacotherapy have been tested in the effectiveness of treating cocaine dependency, yet there is no indication as to which drug category has been shown to be most successful throughout treatment. The various categories that have been tested include antidepressants, anticonvulsants, antabuse, analeptics, glutamate inhibitors, anti-inflammatory, and various others, and no single category has been more effective than others (Karila et al, 2008).

D. Significance

A protocol for treating cocaine dependent individuals is necessary to reduce cocaine use and abuse. This conceptual meta-analysis examines the various categories of psychopharmacotherapy, when combined with behavioral therapy in comparison to behavioral therapy alone in the efficacy of treating cocaine dependency. Overall these treatments will be examined in order to provide a general overview of the methods and efficacy in order to determine what is the best approach.

E. Hypothesis

It is therefore hypothesized that if a cocaine dependent individual is treated with a combination of psychopharmacological and behavioral therapy, then that individual will have more success in reducing cocaine use than if the individual is treated with only behavioral therapy.

1. Operational Definitions

Robyn Liebman

a. Cocaine Dependence

The American Psychiatric Association (*DSM-IV-TR*) describes 7 symptoms for cocaine dependence (2000). If the participant has any three of them they are considered dependent on cocaine. These symptoms include; demonstrating excessive or inappropriate use of cocaine, preoccupation with cocaine, having an increased or decreased tolerance to cocaine, having trouble stopping or reducing drug use once started, withdrawal symptoms when cocaine intake is reduced or stopped, continuing use of cocaine even though it causes issues within everyday life, and sacrifice of important activities or friendships because of cocaine use. All of the studies require that the participants meet the criteria for this diagnosis of cocaine dependence.

The independent variables are the treatment conditions, psychopharmacology and behavioral therapy versus behavioral therapy alone. The treatment success is the dependent variable and will be measured by utilizing the number of participants who have reduced cocaine use. Cocaine use in every study is measured through urine samples provided by participants. These samples are tested for benzoylecgonine, a cocaine metabolite that would indicate that the individual had cocaine in his or her system (Alvarez, Farre, Fonseca & Torrens, 2009). Numerous other studies also assessed cocaine use through self-report of the participants as well as retention in the study.

b. Psychopharmacotherapy

Psychopharmacotherapy is defined as a medication-based therapy that utilizes medication in order to address the underlying pathophysiology of cocaine dependency (Johnson, Roache, Ait-Daoud, Javors, Harrison, et al., 2006).

c. Behavioral Therapy

Behavioral therapy consists of cognitive behavioral therapy (CBT), contingency management (CM), or a combination of the two (Garcia-Rodriguez et al., 2009). Each study specifies the measurements that are utilized within the specific experiment, and that will be clarified throughout the results section. The meta-analysis assesses CBT and CM as forms of behavioral therapy and does not discriminate between the two to determine which one is more effective when combined with psychopharmacotherapy.

II. Results

Many studies have shown that the use of psychopharmacotherapy in combination with behavioral therapy decreases cocaine use in individuals who are dependent. Some of these empirical studies have tested multiple different types of medications, while others look at one. The studies indicate how significant the difference was between the control group, behavioral therapy alone, and the experiment groups, which consisted of behavioral therapy with psychopharmacotherapy.

106 e-Research, Vol 1, No 2 (2010)

A. Attention Deficit Disorder Treatment

Methamphetamine is a stimulant psychopharmacological agent that is most often prescribed to those who suffer from Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder. This psychoactive drug increases levels of dopamine, norepinephrine, and serotonin and is often abused as high levels create a euphoric feeling. The FDA has approved the use of Desoxyn, the trademark name for methamphetamine, in small doses that are taken in an immediate or sustained release form (Mooney, Herin, Schmitz, Moukaddam, Green, & Grabowski, 2009). The use of methamphetamines is hypothesized to be effective in the treatment of cocaine dependency due to the similar mechanism of action.

Participants were randomly assigned to one of three conditions, methamphetamine sustained release, immediate release, or a placebo condition. Each group received CBT throughout the entire trial, and a CM program was added to the behavioral therapy at week five. Cocaine use was measured through urine samples that were collected weekly. The authors hypothesized that the participants that received sustained release and immediate release methamphetamine would produce less cocaine positive samples than the placebo condition. Results indicated a significant difference between the treatment conditions $F(2, 344) = 14.7, p < 0.0001$, the Sustained Release condition decreased positive cocaine urine samples to 29%, immediate release resulted in 66% positive, and the placebo condition 60%. The non-significant results for the immediate release treatment condition can be attributed to the fact that the majority of the doses were not taken and were returned to the clinic. Overall, more research needs to be completed to look at the effects of methamphetamine as a treatment option, along with behavioral therapy, for cocaine dependence. This article supports the overall hypothesis as the sustained release treatment condition along with CBT and CM reduced cocaine use compared to the placebo condition (Mooney et al., 2009).

B. Amyotrophic Lateral Sclerosis Treatment

The only FDA approved medication to treat Amyotrophic Lateral Sclerosis (ALS) is Riluzole. This psychopharmacological agent inhibits presynaptic glutamate release. Cornish et al. (1999) hypothesizes that the glutamatergic systems are involved in the regulation and reduction of drug seeking behaviors in those that are cocaine dependent; therefore riluzole could be an option in treating those drug-seeking behaviors (as cited in Ciraulo et al., 2005). Riluzole was included in a study comparing five different psychopharmacological treatments to a placebo condition, where all conditions received CBT simultaneously. Results were measured through urine analysis provided by the participants. Overall, riluzole, combined with CBT, did not have a significant effect on reducing cocaine positive urine samples, or overall cocaine use by those that are cocaine dependent. These results indicate that riluzole is not an effective treatment, as it did not have a significant outcome compared to the other medications or placebo treatment groups (Ciraulo et al., 2005).

Robyn Liebman

C. Antabuse

Antabuse is a medication traditionally used in the treatment of alcoholism and has also been shown to reduce the breakdown of dopamine in the brain. This mechanism of action suggests that it is efficacious in the treatment of cocaine dependence. At first Disulfiram, an antabuse, was used to treat co-morbid alcohol and cocaine dependence (Carroll, Nich, Ball, McCance, Rounsavile, 1998). However, it is hypothesized that disulfiram may be effective in the treatment of cocaine dependence, regardless of co-morbid alcohol dependence. Medication and cognitive behavioral therapy were tested in the efficacy of treating participants who are solely cocaine dependent. Two types of behavioral therapy, CBT and interpersonal psychotherapy (IPT), were tested along with the medication conditions. Researchers used a 2x2 factorial design, which allowed four treatment groups; disulfiram plus CBT, disulfiram plus IPT, placebo plus CBT and placebo and IPT. Results were measured utilizing urine toxicology screens and self-report of use. The hypothesis stated that, if a cocaine dependent individual was treated with a combination of disulfiram and cognitive behavioral therapy, then there would be greater efficacy than those not treated with disulfiram and cognitive behavioral therapy.

Results of this study showed that the disulfiram and CBT conditions were most efficacious compared to the placebo and IPT conditions. Participants that were treated with medication along with behavioral therapy produced significantly less cocaine samples than those who were in the placebo treatment group ($z = -3.74$, $p < 0.01$). Disulfiram has shown to be efficacious in the treatment of cocaine dependency along with behavioral therapy, although more research is needed in order to determine what type of behavioral therapy best accompanies this psychopharmacotherapy (Carroll et al., 2004).

D. Anti-Convulsant

There are many medications that are prescribed for the treatment of seizures. However, for many of these drugs their mechanism of action is unknown. It is assumed that anticonvulsants would control impulses, often times working through the GABA receptors and dopaminergic system (Alvarez et al., 2009). Gabapentin, Tiagabine, Topiramate, Valproate, Lamotrigine have all been assessed for their efficacy in treating cocaine dependency.

Topiramate, which increases GABA activity in the brain, has been effective in the treatment of other addictions and dependencies, such as alcoholism. In a small study, 40 participants were divided into the control or treatment conditions. The treatment condition received a dose of topiramate each day, which slowly increased over the course of 13 weeks. Every participant received CBT twice a week. Results were measured through urine analysis, and there was a significant difference in the groups, the topiramate treatment condition was more likely to be abstinent from cocaine use over the duration of the study ($Z = 2.67$, $P = 0.01$). This indicates that the odds of cocaine use in the placebo group increased throughout the duration of the study, whereas the odds that the treatment group would use cocaine decreased. Due to the small sample size of this study, it is not clear as to

108 e-Research, Vol 1, No 2 (2010)

whether topiramate is a strong treatment choice for cocaine dependency, although it is promising. More research on this medication should be completed (Kampman et al., 2004).

Two anticonvulsant medications were tested against each other to determine efficacy in the treatment of cocaine dependence. Tiagabine and gabapentin were compared to the placebo control condition in a study utilizing 76 participants. The hypothesis of this study was that if a cocaine dependent individual is treated with either tiagabine or gabapentin, then that individual will have greater efficacy in the reduction of cocaine use than those who receive the placebo. This study is relevant to the overall hypothesis as it tested the efficacy of treating a cocaine dependent individual with medication and cognitive behavioral therapy compared to a placebo and cognitive behavioral therapy. The results were measured through urine samples and self-reported cocaine and indicated that tiagabine had significantly more cocaine-free samples than the gabapentin or placebo treatment conditions. Tiagabine had mean of 43% cocaine-free samples, gabapentin resulted in 31%, and the placebo condition had 35% (Gonzalez et al., 2007).

Tiagabine was also tested in an 8-week trial compared to sertraline and donepezil, that divided a sixty-seven participant sample size into 17 participants per treatment. Each participant received CBT simultaneously. Although results were not significant, tiagabine resulted in less positive urine samples than the other two medications, and the placebo condition. Tiagabine resulted in 73% less positive urine results, compared to the placebo condition which had a 32% increase in positive urine samples. The results for the efficacy of tiagabine as a psychopharmacological treatment, combined with behavioral therapy, in the treatment of cocaine dependency are mixed and need to be researched further in order to determine whether or not tiagabine should be used to treat patients (Winhusen et al., 2005).

Results reported by Gonzalez et al. (2007) indicate that gabapentin was not effective, however, other studies have tested the efficacy of gabapentin in the treatment of cocaine dependency. Gabapentin is known to increase GABA levels in the human brain (Petroff et al., 1998). In one study involving gabapentin, Ninety-nine participants were randomly assigned into either the gabapentin 3200 mg per day treatment or the placebo condition for twelve weeks. Every participant in both treatment conditions also received weekly behavioral therapy, which included cognitive behavioral relapse-prevention therapy. Results of this study indicated that there was no significant difference in cocaine use between treatment conditions ($z = -1.25, .22$). Participants were classified into either a low-use or high-use group depending on their reported cocaine-use during a two-week lead in period. Out of these two classifications, those in the high-use group reduced cocaine use across both treatments. The low-use classification group on average maintained levels of cocaine-use across treatments. These results indicate that those who have a high-level of cocaine use will reduce cocaine-use when receiving cognitive behavioral therapy independent of psychopharmacological therapy. These findings refute the overall hypothesis because there is no significant difference between those treated with psychopharmacology and behavioral therapy compared to those treated with placebo and behavioral therapy (Bisaga et al., 2006).

Robyn Liebman

.....
Another study testing gabapentin, and other medications, found that gabapentin did not result in a significant change in cocaine-negative urine samples compared to the placebo condition, when combined with behavioral therapy. Three medications were evaluated in this study and individuals were placed into one of four conditions, one of the three pharmacotherapies or the placebo. The authors hypothesized that if a cocaine dependent individual is treated with a combination of psychopharmacotherapy and behavioral therapy then it will be more effective than the placebo condition. Results indicated that gabapentin did not produce significant changes in positive urine results, compared to the placebo condition. Gabapentin has not been efficacious in the treatment of cocaine dependency when combined with behavioral therapy, despite what researchers hypothesized based on the effect that gabapentin has on the GABA neurotransmitter levels (Berger et al., 2005).

Valproate, another anti-convulsant, was tested in the treatment of cocaine dependency. This medication has an unknown mechanism of action, but it does enhance GABA levels. In a study examining how effective Valproate is in the treatment of cocaine dependency compared to a placebo condition, each participant was placed into a treatment or placebo group and received CBT throughout the 8-week study. Overall, results indicated that there was no difference in reducing cocaine-negative urine samples between the treatment and placebo conditions. Each group demonstrated overall improvement, however none of the conditions were significantly different than the others. Although there were no significant differences between groups, there is a need for more research in the treatment of cocaine dependency using valproate, as it did lead to a decrease in cocaine positive urine samples overall, along with all the other treatment conditions (Reid et al., 2005a).

In another study, valproate was tested with four other medications and a placebo condition, for its efficacy in the treatment cocaine dependency along with CBT. Sixty-eight participants were randomly assigned to valproate, one of the three psychopharmacological agents, or the placebo condition while concurrently receiving CBT. Results were measured through urine analysis and there was no significant difference in the reduction of cocaine use across treatment conditions. Although the valproate treatment condition has reduced overall cocaine use, when combined with behavioral therapy, the results have not been significant, indicating that valproate may not be the best psychopharmacological agent in treating cocaine dependency (Reid et al., 2005b).

Anti-convulsants have been highly tested in the treatment of cocaine dependency. Although many of the studies indicated that there was no difference between treatment conditions, there is a need for more research utilizing behavioral therapy in combination with anti-convulsants. The results did not show that they increased cocaine use, one study demonstrated that the anti-convulsant reduced overall cocaine use, as did the other psychopharmacological treatment conditions (Reid et al., 2005b).

E. Anti-Depressants

110 e-Research, Vol 1, No 2 (2010)

The use of anti-depressants for the treatment of cocaine dependency has been thoroughly examined. There are three types of anti-depressants that have been studied, which work on different neurotransmitters.

1. Selective Serotonin Reuptake Inhibitor

The first one to address is the selective serotonin reuptake inhibitors (SSRI). These anti-depressants have shown mixed results, as they are effective in rats, but have not been effective in human cocaine dependence treatment. Overall 157 individuals with cocaine dependency were randomly assigned to receive 20 mg of citalopram or a placebo medication for 12 weeks, along with behavioral therapy. Two types of behavioral therapies were assessed, cognitive behavioral therapy and contingency management, which were combined with the medication treatment conditions. The amount of cocaine was measured through urine samples collected from the participants in both treatment conditions. The medication treatment effect was significant compared to the placebo condition; the mean number of consecutive cocaine free days was 5.06 for the treatment condition and 2.13 for the placebo. Those that received the citalopram 20 mg per day and the behavioral therapy produced less positive urine samples than those who received the placebo medication along with the behavioral therapy. Overall the results strongly supports the hypothesis that psychopharmacotherapy combined with behavioral therapy is an effective treatment for cocaine dependency (Moeller et al., 2007).

Another SSRI, sertraline, was tested, along with CBT for efficacy in treating cocaine dependency. This serotonin 5-HT reuptake inhibitor is traditionally used to treat depression, obsessive-compulsive disorder, and panic disorders. Two other psychopharmacotherapies and a placebo condition were also used as grouping variables so samples sizes were n=17. Participants were assessed through urine samples throughout the 8-week trial. The sertraline did not show significant differences in positive urine samples compared to the placebo and other medication treatment conditions. However, altogether each treatment condition was very similar, showing that there was an overall decrease in positive urine samples, none of which were significant (Winhusen et al., 2005).

One other SSRI that was examined is paroxetine. This medication was measured in comparison to four other medications and a placebo condition. Ciraulo et al. (2005) hypothesized that if the cocaine dependent participant was treated with a psychopharmacological agent along with behavioral therapy, then that participant would be more successful in producing less cocaine positive urine results. Each participant received CBT along with the medication or placebo, based on random assignment. Efficacy was measured by urine samples and self-report. Paroxetine did not show a significant difference in efficacy of treatment compared to the other treatment and placebo conditions. Overall, one SSRI was effective when combined with behavioral therapy in the treatment of cocaine dependence. Therefore the results for the SSRI category were mixed. Although other medications did not support the hypothesis, by demonstrating a non-significant response, SSRI medications should still be researched further as a treatment option for cocaine dependency (Ciraulo et al., 2005).

Robyn Liebman

2. Serotonin and Norepinephrine Reuptake Inhibitor

Another category of anti-depressants is the serotonin and norepinephrine reuptake inhibitor, assumed to inhibit serotonin and norepinephrine reabsorption. Venlafaxine was examined in comparison to four other medications and a placebo condition, and all participants received behavioral therapy concurrently. Participants provided urine samples and self-report questionnaires in order to determine cocaine-use. Venlafaxine was not effective when combined with behavioral therapy in reducing cocaine use in participants that are dependent (Ciraulo et al., 2005).

3. MAOI

Lastly, monoamine oxidase inhibitors (MAOI) were assessed in the treatment of cocaine dependency. MAOI's are hypothesized to increase levels of dopamine, serotonin and norepinephrine by breaking down the neurotransmitters. Three hundred participants were randomly assigned to be in the placebo or treatment condition. Selegiline was administered through patches every day, and the placebo condition received a placebo patch instead of the treatment. Each was also supplied with behavioral therapy once a week, despite treatment condition. Cocaine use was measured through urine samples supplied by the participants. Results indicated that both treatment conditions decreased cocaine use among participants. However there was no significant difference between groups. Although there was no significant difference, it is important to note that both conditions had a decrease in cocaine use (Elkashef et al., 2006).

F. Anti-Emetic

Ondansetron is a dopamine receptor antagonist, and has the potential of eliminating the reinforcing effects of cocaine. By eliminating the reinforcing effects, individuals will be less probable to relapse. Therefore this psychopharmacological agent is worth studying in order to determine the efficacy in treating cocaine dependence. It is hypothesized that if ondansetron, with CBT, is used to treat cocaine dependence, it will be more effective than treating solely with CBT. Sixty-three participants were divided into one of four psychopharmacotherapy treatment groups; 0.25 mg, 1.0 mg, 4.0 mg and placebo. Each participant received weekly CBT and urine samples and self-report measures were collected on a weekly basis to assess the efficacy. The 4.0 mg treatment condition showed a significant rate of change compared to the placebo condition. The other two experimental conditions did not show a significant difference from the placebo condition, indicating that more research needs to be completed in order to determine the most effective dosage of ondansetron, along with behavioral therapy, in the treatment of cocaine dependence (Johnson et al., 2006).

G. Anti-Hypertension

.....

Reserpine, a medication used since the 1950's to treat hypertension, was assessed for success in treating cocaine dependency, with a combination of behavioral therapy. This psychopharmacological agent disrupts storage of catecholamines, dopamine and norepinephrine, releasing these neurotransmitters to be metabolized quickly, therefore depleting dopamine until new vesicles become available, which could take several weeks. Therefore, when individuals who are taking reserpine use cocaine, they will no longer experience the euphoric effects of the drug. One study divided participants into two treatment conditions, those that received reserpine and those that received the placebo medication. Along with the psychopharmacological treatment, each participant received weekly, individualized CBT. A total of 79 participants completed the 12-week trial and cocaine use was measured through urine analysis and self-report of craving. No significant outcomes were measured across treatment conditions. Those that received the placebo or the reserpine psychopharmacotherapy, along with CBT, did not result in any significant change of cocaine-positive urine samples over the course of the 12-week study (Winhusen et al., 2007).

Another study conducted on the effectiveness of reserpine compared this medication to three other psychopharmacotherapies over the course of 10 weeks. Participants were assigned to one of four treatment conditions, where they received a placebo, reserpine or one of the other two treatments. All of the subjects participated in individual weekly CBT along with the psychopharmacological treatment. The authors stated that individuals who were treated with a combination of psychopharmacotherapy and behavioral therapy would be more successful in reducing cocaine positive urine samples compared to the placebo and behavioral therapy condition. Results were measured through urine analysis collected weekly and self-report. The reserpine treatment condition, along with CBT, yielded a significant decrease in cocaine positive urine samples. The reserpine and placebo conditions were the only treatments to show a significant change in the amount of cocaine positive urine samples (Berger et al., 2005).

These mixed findings for reserpine indicate that more research should be completed on this psychopharmacological agent. Between the two studies, the treatment time and the subject pools were different and this could be attributed to the difference in results. It is important to further investigate this medication, as it has shown potential for being efficacious in the treatment of cocaine dependency when combined with behavioral therapy.

H. Anti-Inflammatory

Celecoxib is an anti-inflammatory medication that is mainly used to treat arthritis. This medication was tested for the treatment of cocaine abuse because this psychopharmacological agent creates an enhanced sensitivity to cocaine. It works by inhibiting clooxygenase-2 activity, which in turn will affect the level of neuroplasticity in the brain of an individual who chronically uses cocaine. It has been hypothesized that regular cocaine use can cause neuroplasticity, or neuroadaptations, in areas of reward-related learning and memory processes, which in turn can

Robyn Liebman

lead to impulsive decision making and abnormal habits that are not sensitive to negative consequences of these actions (Thomas, Kalivas & Shaham, 2008). Twenty-three participants were divided into two treatment conditions, celecoxib and placebo. Each participant received a cognitive behavioral treatment program throughout the 8-week trial. Results were measured through urine samples and indicated that there was no significant difference between treatment conditions for those treated with celecoxib compared to the placebo condition. Both treatment conditions demonstrated a decrease in cocaine use overall, but there was no difference between the groups in that change. The use of celecoxib and behavioral therapy has not been shown to be efficacious although more studies should be conducted on other types of anti-inflammatory medications (Reid et al., 2005a).

I. Anti-Narcoleptic

A wake-promoting agent used in the treatment of narcolepsy has been effective in the treatment of cocaine dependence in combination with behavioral therapy. Modafinil can help in various ways; first of all it is a stimulant and therefore would alleviate some withdrawal symptoms. Secondly, modafinil has been effective in the treatment of Attention Deficit Hyperactivity Disorder through the glutamate/GABA and hypocretin systems (Anderson et al., 2009). Another empirical study that tested the effects of modafinil on 62 participants found that there was a significant difference between treatment conditions (Dackis, Kampman, Lynch, Pettinati, O'Brien, 2005). There were two treatment conditions, including modafinil 400 mg and the placebo condition. Each participant received twice-weekly CBT. Results indicated that there was a significant difference between treatment conditions. The modafinil plus cognitive behavioral therapy condition resulted in significantly less positive urine samples over the course of 8 weeks. The mean percentage of negative urine samples was 42.3% for the medication treatment condition and 24.0% for the placebo treatment. Overall, supporting the hypothesis that psychopharmacotherapy plus behavioral therapy is more effective in producing less positive urine samples than therapy alone.

Another experimental study hypothesized that modafinil plus CBT treatment would be more successful in reducing cocaine use in those that are cocaine dependent compared to participants that were given the placebo condition. Three treatment conditions were tested; modafinil 200mg, 400 mg, and placebo. Along with these medication treatments, each participant underwent one hour of manually guided CBT each week. The rate of change between treatment conditions was not significant, however the maximum number of consecutive non-use days was significant. The average number of non-use days; 400 mg modafinil averaged 12.0 days, 200 mg averaged 12.6 days, and the placebo condition averaged 8.8 days. Those that were in the modafinil treatment conditions had a significantly higher amount of consecutive non-use days compared to the placebo condition. This supports the hypothesis that a combination of psychopharmacotherapy and CBT can reduce the number of non-use days (Anderson et al., 2009).

J. Anti-Parkinson

114 e-Research, Vol 1, No 2 (2010)

.....

Levodopa is a medication used to treat Parkinson's Disease. It works as a dopamine precursor. Due to the effect that levodopa has on dopamine in the brain, it is hypothesized that it will be efficacious in the treatment of cocaine dependency, as it could help reduce cravings and chronic use. The study by Schmitz et al. (2008) also tested the efficacy of levodopa with three different types of behavioral therapy; clinical management, CBT, and voucher-based reinforcement (CM). This was a 3x2 study and therefore participants were divided into 6 different treatment conditions. Cocaine use was measured through urine analysis collected three times per week. Overall, there was a significant reduction in cocaine use in the Levodopa (M = 61.6%) compared to the placebo condition (M = 79.1%), despite what type of behavioral therapy was used. The voucher-based reinforcement treatment condition combined with levodopa had the lowest cocaine positive samples (M = 59%), compared to CBT and levodopa (M = 84%), however each behavioral therapy condition was significantly lower combined with the levodopa than with the placebo. This study supports the hypothesis that behavioral therapy combined with psychopharmacotherapy is the most effective treatment option in reducing cocaine use among those that are dependent (Schmitz et al., 2008).

Levodopa-Carbidopa is a combination of levodopa, which is a precursor of dopamine, and a decarboxylase inhibitor, which increases dopamine activity. The theory behind using L-dopa is that it will stabilize dopamine stores, which are often depleted with the chronic use of cocaine. The first treatment condition received 200/50 mg of L-dopa, which doubled to 400/100 mg by the end of the trial, and the second received 400/200 that doubled to 800/200 mg. The third treatment condition received a placebo throughout the entire 8 weeks. Every participant in each treatment condition received 1 hour of cognitive behavioral therapy each week as well as the medication or placebo. The hypothesis states that the L-dopa treatment condition will be more efficacious on treating those with cocaine dependence than the placebo condition. The outcome of this study indicated that there was no significant difference in the percentages of cocaine use of the L-dopa treatment (40.0%) compared to the placebo (51.0%) conditions. Urine levels were not significantly different across treatments, despite time in treatment or medication dose. Although the differences in cocaine use were not significant across treatment conditions, there was a slight decrease in the L-dopa treatment group, which suggests that more studies should be conducted in order to determine whether L-dopa could be an effective treatment in combination with behavioral therapy (Mooney et al., 2007).

In a study comparing levodopa-carbidopa to two other medications and a placebo condition, participants were randomly assigned to a medication treatment condition and received weekly CBT treatment for the 8-week trial. Urine screenings and self-report was used to evaluate cocaine use and were collected three times per week. Shoptaw et al. (2005) hypothesized that if a participant received one of the medications along with behavioral therapy, then that participant would demonstrate higher reduction in cocaine use than those in the placebo condition. However, results did not indicate a significant difference in the reduction of cocaine use between the levodopa-carbidopa group and the placebo group (Shoptaw et al., 2005). Levodopa should be further examined as the results indicate mixed results in the efficacy of reducing cocaine use.

Robyn Liebman

A third type of medication used to treat Parkinson's disease is called pramipexole, which is a dopamine agonist. As seen before, this study tested this psychopharmacological agent along with four others. Pramipexole was one medication that was compared to a placebo condition to assess the efficacy in reducing cocaine use. Each participant received CBT along with the psychopharmacological or placebo treatment. Results were measured through urine analysis and self-report. Pramipexole did not reduce cocaine use significantly compared to the other treatment conditions (Ciraulo et al., 2005).

Anti-Parkinson medications have a mechanism of action that work as either an agonist or precursor to dopamine (Schmitz et al., 2008). Because of this action, it has been hypothesized that these medications will have a significant effect on the treatment and reduction of cocaine use in individuals who are dependent on cocaine. However, after examining Levodopa, Levodopa-carbidopa and pramipexole there have mixed results that indicate that these psychopharmacological agents could be affective, in combination with behavioral therapy, in the treatment of cocaine dependence.

K. Anti-Psychotic

Atypical antipsychotic medications are a second generation of antipsychotics that work with the dopamine system, although the specific mechanism of action for these medications is unknown, and differs between each one (Reid et al., 2005b). One anti-psychotic in particular, olanzapine, has an unknown mechanism of action, but has been hypothesized to be a dopamine antagonist. This type of psychopharmacological agent can be effective in the treatment of cocaine dependence because it would potentially assist in cocaine cravings of those individuals that are dependent. One study utilized examined the efficacy of olanzapine compared to three other psychopharmacological treatments and a placebo condition. A total of 68 participants were randomly assigned to one of the five medication treatment conditions, and each participant received CBT counseling throughout the treatment. Efficacy of the treatment conditions was measured through urine analysis collected from the participants. Results demonstrated that there were no significant changes across treatment conditions in the reduction of cocaine positive urine samples. These results indicate that the use of olanzapine is not efficacious, when combined with CBT, in the reduction of cocaine use in those that are dependent on cocaine.

L. Arterial Obstruction

Pentoxifylline is a phosphodiesterase inhibitor that increases blood flow and is mainly used to treat patients with muscle pain or fatigue. It is hypothesized to be effective in the treatment of cocaine dependency, as it will suppress the self-administration of cocaine in those who are dependent. This psychopharmacological agent was compared to four other medications and a placebo condition, combined with CBT in the efficacy of reducing cocaine positive urine samples. Results indicated that over the 8-week trial, pentoxifylline, combined with CBT, did not have a significant effect on reducing cocaine use in participants who are considered cocaine dependent. These

116 e-Research, Vol 1, No 2 (2010)

results refute the overall hypothesis and there was no significant difference between psychopharmacological and placebo treatment conditions (Ciraulo et al., 2005).

M. Dementia

Hydergine is a medication used to enhance cognition and improve memory in those patients that suffer from dementia. Although the mechanism of action for hydergine is unknown, it is assumed that it increases cerebral glucose metabolism in the cortex, enhance cerebral blood flow, and effect selective dopamine receptor sites. In an experimental study over 8 weeks, cocaine dependent participants were randomly assigned to one of four treatment conditions, including a placebo treatment; each treatment conditions had 15 participants. Each participant also underwent CBT throughout the trial. Measurements of the efficacy of the psychopharmacological agents were assessed through urine analysis and self-report. Results indicated that the participants in the hydergine treatment condition produced more negative cocaine urine samples compared to the placebo, however the difference was not significant. Hydergine, however, was the only medication out of the three tested in this experiment to demonstrate a decrease in urine positive results, although not significant. These results lead to the conclusion that hydergine should be further examined, in combination with behavioral therapy for the treatment of cocaine dependent individuals (Shoptaw et al., 2005).

N. Hyperprolactonemia

Hyperprolactonemia is a disease that causes excessive levels of proactin in the blood. Webster et al. (1994) states that cabergoline is mainly used to treat those with this disorder and has been shown to bind to dopamine receptors and inhibit the release of proactin secretion (as cited in Shoptaw et al, 2005, p. 79). The use of cabergoline has also been effective in the improvement of motor functions for those suffering from Parkinson's disease. In a study comparing cabergoline to two other medications and a placebo condition, 60 participants were randomly assigned into four treatment conditions. Each treatment condition received CBT treatment as well, and urine samples were utilized to assess the efficacy of the psychopharmacological treatments in comparison to the placebo condition in reducing cocaine use in the participant pool. Results indicated that the cabergoline treatment condition produced significantly less positive urine samples (55.8%) compared to the placebo condition (38.6%; $F = 4.02$, $df = 3$; $P = 0.02$). These results are significant and indicate that cabergoline could be an effective treatment, combined with CBT, in the treatment of cocaine dependency by reducing use among participants. Although this study indicated that results were significant, more research in order to replicate this study should be completed (Shoptaw et al., 2005).

O. Muscle Relaxant

Baclofen is a psychopharmacological agent that is a GABA receptor agonist that is a skeletal muscle relaxant. It is most commonly prescribed for multiple sclerosis, spinal cord disease and injury. Baclofen is hypothesized to effect

e-Research, Vol 1, No 2 (2010) **117**

Robyn Liebman

cocaine-evoked dopamine release, therefore would be able to reduce cocaine use and cravings in those that are dependent on cocaine. A study comprised of 160 subjects was divided into two treatment conditions, one placebo condition and one where the participants received baclofen. Every participant despite treatment condition also received weekly CBT therapy for one hour. This study was 8 weeks long and results were measured through urine samples. Results of the urine analysis indicated that baclofen did not have a significant impact on the amount of cocaine-negative urine samples compared to the placebo condition. Overall this particular psychopharmacological agent, combined with behavioral therapy did not have a significant impact on cocaine use in individuals that are dependent, however muscle relaxants should not be ruled out completely for the treatment of cocaine dependence (Kahn et al., 2009).

P. Vitamins and Supplements

The use of vitamins and supplements in the treatment of cocaine dependency has not been widely tested. Many researchers focus on those psychopharmacological agents that are produced by drug companies to treat major illnesses. However, it is worth examining these vitamin and supplements to see if there they have any impact on cocaine use in those that are dependent.

Chronic cocaine use may impact cell membranes and lead to damage, a consequence of mitochondrial dysfunction, which is caused by impairment of cerebral metabolism. Coenzyme Q10 (CoQ10) is a substance that is found in the mitochondria and is an important component of the electron transport chain, participating in aerobic cellular respiration. Corwin et al., 1998 argues that without CoQ10, there can be mitochondrial dysfunction, which could possibly lead to cell membrane damage, which would in turn cause neuronal degeneration (as cited in Reid et al., 2005b, p. 45). This degeneration could then cause neuropsychological deficits, leading to the reduction in impulse control in those that use cocaine frequently. Therefore, the CoQ10 supplement is tested for efficacy in the ability to reduce cocaine use to determine its efficacy in treating cocaine dependence. CoQ10 was tested along with two psychopharmacological agents and a placebo condition. Participants were randomly assigned to one of the four conditions and received simultaneous CBT treatment. Results indicated that there were no significant differences in the CoQ10 treatment condition compared to the placebo condition regarding negative cocaine samples. The self-reported cocaine use however decreased in all treatment groups but there were no significant differences between conditions. The use of CoQ10 in combination with behavioral therapy was not shown to be effective or supportive of the overall hypothesis that a combination of pharmacotherapy and behavioral therapy would be more effective in the treatment of cocaine addiction than the behavioral therapy treatment alone (Reid et al., 2005b).

Cocaine has been shown to alter the serotonin levels in the brain as well as the dopamine levels. Although many studies have looked at the results of altering the dopamine system, research on the serotonin system is equally important. Tryptophan, an amino acid that is ingested has been shown to increase production of serotonin.

118 e-Research, Vol 1, No 2 (2010)

Therefore, tryptophan has the potential to assist in the treatment of cocaine dependency, when combined with behavioral therapy in order to reduce cocaine use, which is argued by Herges & Taylor, 1998 (as cited in Jones et al., 2004, p. 422). This particular study by Jones et al. (2004) uses CM in combination with tryptophan to treat cocaine dependence. This 2x2 study tested tryptophan versus placebo conditions and contingent vouchers versus non-contingent vouchers. Participants were randomly assigned to one of the four treatment conditions for a 16-week trial. Results were measured through urine samples that were collected three times per week. The results indicated that there was no significant difference in the medication treatment condition compared to the placebo. However, there was a significant difference between therapy conditions. The contingent voucher therapy yielded less positive urine results compared to the non-contingent voucher therapy. Although these results do not support the overall hypothesis, they do reinforce the idea that CM is an effective type of behavioral therapy, and when combined with an efficacious psychopharmacological agent can be a successful treatment for cocaine dependency.

Dehydroepiandrosterone (DHEA) is an adrenal steroid hormone that is available over the counter in the United States. Shoptaw et al. (2004) looked at the efficacy of DHEA in the treatment of cocaine dependency. Fifty-seven participants were randomly assigned to either receive DHEA 100 mg per day or a placebo treatment. Along with the medication, participants received cognitive behavioral group therapy three times per week. The hypothesis of this article states that if cocaine dependence is treated with DHEA combined with behavioral therapy, then there would be less positive urine samples than those who received the placebo and cognitive behavioral therapy treatment. The results of this article indicate that there was a significant difference between conditions. The placebo group had significantly more cocaine negative urine samples (70.6%) than the DHEA treatment condition (26.8, $p < .01$). This strongly refutes the overall hypothesis as the psychopharmacological and behavioral therapy treatment condition produced less negative urine samples than the placebo and behavioral therapy condition. DHEA has shown to be not effective in the treatment of cocaine dependence and directly refutes the overall hypothesis.

Discussion

A. Summary of Findings

Overall the findings varied amongst all of the empirical studies reviewed. Some types of psychopharmacological agents were shown to be effective, when combined with behavioral therapy in the treatment of cocaine dependency while others did not demonstrate a significant difference between the placebo and treatment conditions (Appendix A). Although there is a greater number of medications that had no significant impact on the reduction of cocaine use than those that reduced cocaine use, the implication that some psychopharmacotherapies assisted in the reduction of cocaine use is vital in the formulation of a protocol for treating cocaine dependence. The results of this conceptual meta-analysis lead to implications that if a cocaine

Robyn Liebman

dependent individual is treated with a combination of psychopharmacotherapy and behavioral therapy, then that person will be more successful in reducing dependency than if only treated with behavioral therapy.

1. Support

The psychopharmacological treatments that were most effective in reducing cocaine use were the monoamine and GABA enhancers. These medications have a mechanism of action that increases the monoamine and GABA levels in the brain. For example, methamphetamine reduced cocaine use based on urine analysis (Mooney et al., 2009). This medication was one of the more effective medications that was tested with behavioral therapy, compared to the placebo condition. Mooney et al. discovered that sustained release tablets of methamphetamine significantly reduced cocaine use among participants (2009). Another psychopharmacological agent, modafinil, which is a wake promoting agent that releases dopamine and norepinephrine into the brain, was also considered highly effective in the treatment of cocaine dependency, which was demonstrated within two experiments (Anderson et al., 2009; Dackis et al., 2005).

Anti-convulsant medications, that are traditionally used to treat seizures, were also efficacious in reducing cocaine use throughout multiple studies. The most successful of these medications was tiagabine and topiramate, which both are hypothesized to increase GABA through transport inhibition (Gonzalez et al., 2007; Kampman et al., 2004; Winhusen et al., 2005). Although the mechanism of action for anti-convulsant medications is not specifically known, it is predicted that they increase GABA levels. These GABA levels are vital in order to control impulses for those that are dependent on cocaine, therefore reducing times of cocaine usage which will lead to a successful treatment (Alvarez et al., 2009).

Levodopa, a medication used to treat Parkinson's disease, is proven to be a precursor for dopamine levels, and has also shown efficacy in the treatment of cocaine dependence (Schmitz et al., 2008). Overall those medications that impacted GABA and monoamine neurotransmitters in the brain were most effective in reducing cocaine use in those that are dependent.

2. Refute

Along with support for the hypothesis there are also numerous psychopharmacological options that, when combined with behavioral therapy, do not have a significant impact on the treatment of cocaine dependence. Two separate types of refutations were revealed. The first of these refutations is the treatment conditions that had no significant effect on reducing cocaine use, compared to the placebo condition when combined with behavioral therapy. Often times the placebo and treatment conditions led to a decrease in cocaine use, but the difference between the two conditions was not significant (CITATION). The second type of refutation is less common, and implies that the use of psychopharmacotherapy with behavioral therapy increased the amount of cocaine use

120 e-Research, Vol 1, No 2 (2010)

within the individual compared to the placebo condition. This is a direct contradiction to the hypothesis and therefore is the strongest of the refutations.

The medications that refute the hypothesis, by not demonstrating a significant change in cocaine use include; muscle relaxants, dementia medications, anti-inflammatories, MAOI's and SNRI's. There were no medications within these categories that were shown to be significantly effective. An example of this is seen in a study conducted by Reid, Cadastrone et al., (2005) when celecoxib, an anti-inflammatory, was assessed for efficacy in treating cocaine dependence. Both of the conditions, the placebo and experimental, reduced levels of cocaine use, however the difference between the two conditions was not significant.

One psychopharmacological treatment yielded results that directly disproved the hypothesis and yielded more cocaine use among individuals. The androgenic steroid, dehydroepiandrosterone, increased cocaine use among participants that were in the experiment condition compared to the placebo (Shoptaw et al., 2004). This psychopharmacological agent directly challenges the hypothesis. This psychopharmacological agent disproves the hypothesis as it demonstrated an increase in cocaine use among participants. Therefore this medication treatment is a strong refutation of the overall hypothesis that a combination of psychopharmacological and behavioral therapy will be more successful in the reduction of cocaine use, compared to behavioral therapy alone.

In summary of these findings, medications that enhance monoamine and GABA levels in the brain have been efficacious in the treatment of cocaine dependency, as measured through the reduction of cocaine use in participants that are dependent.

B. Strengths and Limitations

Each study included the strengths and weaknesses specific to the measurements, participation sizes, dropout rates and other various items. However many of the studies had similar strengths and weaknesses, which are important to note in the evaluation of these treatments so as to determine which type of treatment should be used to eliminate cocaine dependency, when combined with behavioral therapy.

1. Strengths

Throughout the various empirical studies, there have been numerous strengths indicating that results could have an impact on how cocaine dependency is treated in the future, one of the main strengths was the sizes of the studies. Sample sizes varied across all studies. It is important to have a large enough participant number in order to be able to assess the results in terms of the population that the sample is taken from.

The study that tested the efficacy of selegiline transdermal system had the largest sample size throughout every empirical article researched (Elkashef et al., 2006). Three hundred participants, in total, were divided into two

Robyn Liebman

groups and each treatment condition had 150 subjects. Results indicated that selegiline was not effective, in combination with behavioral therapy, for the treatment of cocaine dependency. This large sample size is strongly supportive of the validity of these results. With a large sample size the results are more easily applicable to the general population.

Another empirical study utilized six different testing sites to test Modafinil, an anti-narcoleptic (Anderson et al., 2009). This study recruited 35 participants per site, totaling 210 individuals recruited. This sample size was large, compared to many other similar studies, and was very diverse due to the six different locations that this study was performed at. This sample size was considered to be adequate for the study, and was larger than most others in this area of research.

An experiment, that tested the efficacy of reserpine, divided 119 participants that met the criteria for cocaine dependency into two different groups, experiment or placebo treatment conditions (Winhusen et al., 2007). The use of a large number of participants and dividing them into only 2 treatment conditions was a strength in this study as more people were examined for the efficacy of reserpine in the treatment of cocaine dependency.

Besides sample sizes, it is important to look at the length of each treatment study. Recovery from addiction is a long process, and many of the psychopharmacological agents that are utilized can take multiple weeks before participants begin to benefit from the effects. All of the articles reviewed were longitudinal studies, and the participants were treated with the behavioral therapy and psychopharmacotherapy everyday for multiple weeks.

One study in particular, completed by Bisaga et al. (2006), was over a duration of 16 weeks. The 16 weeks of treatment allowed for the adjustment of medication levels within the experimental group. By monitoring the participants for 16 weeks, researchers are able to gain a stronger measurement of cocaine use and efficacy of the treatment conditions. The length of this study allowed for the randomization and adequate testing of the effects of the medication.

A handful of studies also had long treatment or maintenance therapies. Averaging around 9.26 weeks of treatment for all 22 empirical articles reviewed. A second trial, conducted by Jones et al. (2004), was also conducted over 16 weeks. Over the duration of the trial, participants received CM vouchers, psychopharmacological treatment, and urine testing twice a week. This longer study is more effective in truly assessing the efficacy of behavioral therapy along with psychopharmacotherapy. Researchers are able to measure the participants over a long period of time, so as to record any significant changes as the medication and therapy have time to positively, negatively, or not affect the participant at all. The average number of weeks that the studies lasted, 9.26, is a strong point to the overall results. Trials are long enough to allow participants to settle into the treatment group that they were randomly assigned to, in order to accurately assess their progress over the trial time.

122 e-Research, Vol 1, No 2 (2010)

Another major strength to the conceptual meta-analysis is the outcome measures that were used in each study. Every study utilized urine testing to determine use of cocaine by the participants. Many trials also examined the self-reports of the participants, collected frequently, to assess the efficacy of the different treatment conditions. The fact that urine was tested in each study indicates a consistent similarity in order to compare the different studies; therefore this is a direct way of measuring each experiment's outcome in comparison to the others. It is important to have the same, or similar outcome measures in order to be able to determine how the studies relate to each other and what the best type of treatment for cocaine dependency is.

Finally, another strength emerged that was only seen in two articles. This strength was the assessment of two or more different types of behavioral therapies in comparison to each other, along with the analysis of the psychopharmacotherapy compared to placebo conditions. Moeller et al. (2007) utilized a 2x2 design to test the interaction difference between treating a patient with CBT versus CM and medication versus placebo conditions. Participants were divided up into one of four treatment conditions, to allow the researchers to determine what was the most effective type of behavioral therapy. Researchers could also determine if the treatment was more effective when it was combined with psychopharmacotherapy.

Schmitz et al. (2008) utilized a 2x3 design to compare the effects of the psychopharmacotherapy administration across three types of behavioral treatments. The three types of behavioral treatments consisted of clinical management only, clinical management plus CBT, or clinical management combined with CBT and CM. This allowed researchers to determine the effects of adding different types of behavioral therapies to the psychopharmacotherapy treatment in reducing cocaine use among those that are dependent.

Although only two of the studies designed experiments that compared the differences between behavioral therapies, they are important to note in the strengths of the overall meta-analysis because they can help determine in the future, which type of behavioral therapy combined with psychopharmacotherapy is most effective in treating cocaine dependence.

2. Limitations

Despite numerous strengths, there were also several limitations to the overall meta-analysis. These limitations may impact the overall results, yet with more research there could be advances in determining the best overall treatment for cocaine dependency.

A prominent limitation across all studies was the dropout rates as well as the missed urinalysis appointments by the participants. Dackis et al. (2005) completed a study that tested the efficacy of Modafinil in treating cocaine dependence and had a significant drop out rate. The total percentage of participants that completed the study was

Robyn Liebman

64.5%. Drop out rates are extremely high in cocaine studies as they are longitudinal studies that require numerous visits per week. Many other studies suffered from this limitation.

Many of the studies contained a small number of participants, therefore limiting the real world implications of the findings. One study, in particular, had 23 participants total complete the study (Reid, Angrist et al., 2005). This small sample size was then divided in half when randomly assigned to treatment conditions. The experimental condition had 10 participants, compared to the placebo condition with 13 participants total. This small sample size is a limitation of the study because each individual has a strong impact on the data, easily manipulating the overall results. More research should be conducted in order to eliminate this limitation with a greater number of participants per treatment condition.

Many of the studies that assessed more than one psychopharmacotherapy in comparison to others had small sample sizes per treatment condition. Berger et al. (2005) divided participants in order to test 3 medications and one placebo condition. Therefore when the study began with a relatively average sample size of $n=60$ the number has an inverse relationship with the number of treatment conditions. This study divided the 60 participants into 4 groups of 15 participants per treatment condition. Each group contained a small sample size, which places limitations on the ability to assess the efficacy of the psychopharmacological agents compared to each other. When the sample size is small, as it is in a few of the studies analyzed, the results become harder to generalize to the large cocaine dependent population in the real world.

Due to the fact that little is known about the best pharmacological treatment option to use for cocaine dependency, some of the empirical articles experimented with more than one category of medication in the trials. This can complicate results, as there is no focus on one type of medication and therefore results are sporadic. Ciraulo et al. (2005) used 5 medications and one placebo condition. These 5 different medications are in different medication categories, and are used to treat an array of ailments. Therefore, results are more difficult to generalize.

Behavioral therapy in this meta-analysis includes two types of therapies, CBT and CM. Due to the broad definition of behavioral therapy, one of the limitations discovered when reviewing the empirical articles was the unbalanced use of both therapies. Many more studies utilized CBT than CM, therefore the efficacy of combining medication with behavioral therapy is limited. There is a possibility that utilizing both behavioral therapies could be more effective than limiting it to one. Another important aspect that limits the ability to compare studies is the number of sessions of behavioral therapy and how the session was operated. Each trial utilized behavioral therapy, however there would be a discrepancy between number of session of therapy. For example one study supplied participants with behavioral therapy three times per week (Shoptaw et al., 2004), compared to another study that treated a participant once a week (Shoptaw et al., 2005). This discrepancy is a limitation in determining the efficacy

of behavioral therapy combined with psychopharmacotherapy compared to behavioral therapy alone in the treatment of cocaine dependency.

C. Conclusions

Overall, results indicated that psychopharmacotherapy and behavioral therapy are shown to be effective when used together. The psychopharmacological agents that have been most effective are the monoamine and GABA enhancers. These include anti-convulsives, methamphetamine, wake-promoting agents, and other medications that enhance GABA and other neurotransmitters such as norepinephrine, serotonin, and dopamine. Cocaine has a very complicated mechanism of action and therefore medications that have an effect on various neurotransmitters are often efficacious in the treatment of cocaine dependency (Streeter et al., 2005). The mechanism of action of cocaine is known, and a trend appears in the types of psychopharmacotherapies that are effective in treating cocaine dependency when combined with behavioral therapy. However, there is no definitive category of medication that seems to be most effective.

D. Impact

Cocaine dependency is a problem across America. The numbers of dependent individuals is astronomically high. The use of cocaine has a negative effect on society and the individual who is abusing the drug. There are numerous problems due to cocaine dependency and these include costs of treatment, social complications, the spread of infectious diseases, and cocaine related crime and violence. By reducing the cocaine dependent population, the problems that this behavior creates will lessen. The results of this meta-analysis indicate that, with more research, there can be a protocol developed to treat cocaine dependency. With this protocol, people will be able to gain better care and treatment and therefore reduce the problems that society faces due to cocaine use.

Throughout the empirical articles researched, a trend developed. This trend is significant to the scientific community to focus future research looking at psychopharmacological treatment options. Researchers have examined numerous medications to treat cocaine dependence, along with behavioral therapy, and this research is combined and organized in a way that could assist those who are conducting experiments with participants. With a focus, research time and money could be reduced when searching for an effective treatment for cocaine dependence.

E. Future Directions

Because of these findings, there is a necessity for the continuation of research on psychopharmacotherapy options that can be added to behavioral therapy treatments to help those who are cocaine dependent. Some medications were efficacious, when combined with behavioral therapy, in reducing cocaine use and therefore this avenue needs to be tested further across different populations, sample sizes, and degrees of dependency.

Robyn Liebman

.....
Further research should focus on specific categories of medication. As stated earlier, one of the limitations was testing the broad range of psychopharmacological categories instead of focusing on one in particular. A study within each medication category, that has shown efficacy, would be beneficial to the overall goal of developing a psychopharmacological agent that could treat cocaine dependency. For example, various SSRI medications should be tested in the same trial in comparison to each other. Instead of spreading out among different medication categories in one study, focusing on a specific medication will help assist researchers in discovering which mechanism of action category is effective in reducing cocaine use. This could further the narrowing down of the broad psychopharmacological spectrum to a certain type, or category, of medication that is most successful.

Two studies that were reviewed focused on testing the types of behavioral therapies, in conjunction with psychopharmacotherapies, in order to determine the best outlet for treatment. Although behavioral therapy is currently the most effective and widely used treatment to treat dependency, one type of behavioral therapy could be more effective, when combined with medication than the others.

Behavioral therapy is a successful option in the treatment of this dependency, however there is a strong potential for the use of psychopharmacotherapy in conjunction with behavioral therapy to more effectively treat cocaine dependence.

References

Alvarez, Y., Farre, M., Fonseca, F., Torrens, M. (2010). Anticonvulsant drugs in cocaine dependence: a systematic review and meta-analysis. *Journal of Substance Abuse Treatment*, (38)1. 66-73

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders (Revised 4th ed.)*. Washington, DC: Author.

Anderson, A., Reid, M., Li, S., Holmes, T., Shemanski, L., Slee, A., et al. (2009). Modafinil for the treatment of cocaine dependence. *Drug and Alcohol Dependence*, 104(1), 133-139. Berger, S., Winhusen, T., Somoza, E., Harrer, J., Mezinskis, J., Leiderman, D., et al. (2005). A medication screening trial evaluation of reserpine, gabapentin and lamotrigine pharmacotherapy of cocaine dependence. *Addiction*, 100(1), 58-67.

Bisaga, A., Aharonovich, E., Garawi, F., Levin, F., Rubin, E., Raby, W., et al. (2006). A randomized placebo-controlled trial of gabapentin for cocaine dependence. *Drug and Alcohol Dependence*, 81(3), 267-274.

Carroll, K.M. (1998). A cognitive behavioral approach: treating cocaine addiction. *Therapy Manuals for Drug Addiction*, 1, 1-12

.....
Carroll, K., Nich, C., Ball, S., McCance, E., & Rounsavile, B. (1998). Treatment of cocaine and alcohol dependence with psychotherapy and disulfiram. *Addiction*, 93(5), 713-727.

Carroll, K., Fenton, L., Ball, S., Nich, C., Frankforter, T., Shi, J., et al. (2004). Efficacy of disulfiram and cognitive behavior therapy in cocaine-dependent outpatients. *Archives of General Psychiatry*, 61(3), 264-272.

Carroll, K.M., & Onken, L.S. (2005). Behavioral Therapies for Drug Abuse. *The American Journal of Psychiatry*, 162(8). 1452-1460

Ciraulo, D., Sarid-Segal, O., Knapp, C., Ciraulo, A., LoCastro, J., Bloch, D., et al. (2005). Efficacy screening trials of paroxetine, pentoxifylline, riluzole, pramipexole and venlafaxine in cocaine dependence. *Addiction*, 100(1), 12-22.

Courtwright, D.T. (1991). The first American cocaine epidemic. *OAH Magazine of History*, 6(2). 20-21

Dackis, C., Kampman, K., Lynch, K., Pettinati, H., & O'Brien, C. (2005). A double-blind, placebo-controlled trial of modafinil for cocaine dependence. *Neuropsychopharmacology*, 30(1), 205-211.

Drug Enforcement Administration (2005). Stimulants. In D. Joseph, (Eds.), *Drugs of Abuse* (31-38). Washington D.C.: U.S. Department of Justice

Elkashef, A., Fudala, P.J., Gorgon, L., Li, S.H., Kahn R., Chang, N., et al. (2006). Double-blind, placebo-controlled trial of selegiline transdermal system (STS) for the treatment of cocaine dependence. *Drug and Alcohol Dependence*, 85(3). 191-197

Friedman, H., Pross, S., Klein, T. W., (2006). Addictive drugs and their relationship with infectious diseases. *FEMS Immunology & Medical Microbiology*, 47(3). 330-342

Garcia-Rodriguez, O., Secades-Villa, R., Higgins, S., Fernandez-Hermida, J., Carballo, J., Errasti Perez, J., et al. (2009). Effects of voucher-based intervention on abstinence and retention in an outpatient treatment for cocaine addiction: A randomized controlled trial. *Experimental and Clinical Psychopharmacology*, 17(3), 131-138.

Gonzalez, G., Desai, R., Sofuoglu, M., Poling, J., Oliveto, A., Gonsai, K., et al. (2007). Clinical efficacy of gabapentin versus tiagabine for reducing cocaine use among cocaine dependent methadone-treated patients. *Drug and Alcohol Dependence*, 87(1), 1-9.

Higgins, S., & Petry, N. (1999). Contingency management: Incentives for sobriety. *Alcohol Research & Health*, 23(2), 122-127.

Robyn Liebman

.....
Higgins, S.T., Dawn, D.D., Budney, A.J., Bickel, W.K., Hughes, J.R., Foerg, F., et al. (2005). A behavioral approach to achieving initial cocaine abstinence. *The American Journal of Psychiatry*, 148(9), 1218-1224.

Hoaken, P.N., & Stewart, S.H. (2003). Drugs of abuse and the elicitation of human aggressive behavior. *Addictive Behaviors* 28(9), 1533-1554

Johnson, B., Roache, J., Ait-Daoud, N., Javors, M., Harrison, J., Elkashef, A., et al. (2006). A preliminary randomized, double-blind, placebo-controlled study of the safety and efficacy of ondansetron in the treatment of cocaine dependence. *Drug and Alcohol Dependence*, 84(3), 256-263.

Jones, H., Johnson, R., Bigelow, G., Silverman, K., Mudric, T., & Strain, E. (2004). Safety and efficacy of L-tryptophan and behavioral incentives for treatment of cocaine dependence: A randomized clinical trial. *The American Journal on Addictions*, 13(5), 421-437.

Kahn, R., Biswas, K., Childress, A., Shoptaw, S., Fudala, P., Gorgon, L., et al. (2009). Multi-center trial of baclofen for abstinence initiation in severe cocaine-dependent individuals. *Drug and Alcohol Dependence*, 103(1), 59-64.

Kampman, K., Pettinati, H., Lynch, K., Dackis, C., Sparkman, T., Weigley, C., et al. (2004). A pilot trial of topiramate for the treatment of cocaine dependence. *Drug and Alcohol Dependence*, 75(3), 233-240.

Karila, L., Gorelick, D., Weinstein, A., Noble, F., Benyamina, A., Coscas, et al. (2008). New treatments for cocaine dependence: a focused review. *The International Journal of Neuropsychopharmacology*, 11(3), 425-38

McKay, J.R., Lynch, K.G., Coviello, D., Morrison, R., Cary, M.S., Skalina, L., et al. (2010). Randomized trial of continuing care enhancements for cocaine-dependent patients following initial engagement. *Journal of Consulting and Clinical Psychology*, 78(1), 111-120

Moeller, F., Schmitz, J., Steinberg, J., Green, C., Reist, C., Lai, L., et al. (2007). Citalopram combined with behavioral therapy reduces cocaine use: A double-blind, placebo-controlled trial. *American Journal of Drug and Alcohol Abuse*, 33(3), 367-378.

Mooney, M., Schmitz, J., Moeller, F., & Grabowski, J. (2007). Safety, tolerability and efficacy of levodopa-carbidopa treatment for cocaine dependence: Two double-blind, randomized, clinical trials. *Drug and Alcohol Dependence*, 88(2), 214-223.

Mooney, M., Herin, D., Schmitz, J., Moukaddam, N., Green, C., & Grabowski, J. (2009). Effects of oral methamphetamine on cocaine use: A randomized, double-blind, placebo-controlled trial. *Drug and Alcohol Dependence*, 101(1), 34-41.

128 e-Research, Vol 1, No 2 (2010)

Musto, D.F. (1989). America's first cocaine epidemic. *The Wilson Quarterly*, 13(3). 59-64

National Drug Intelligence Center (2010). *National Drug Threat Assessment*. Washington D.C.: Department of Justice

Olmstead, T.A., & Petry, N.M. (2009). The cost-effectiveness of prize-based and voucher-based contingency management in a population of cocaine or opiod dependent outpatients. *Drug and Alcohol Dependence*, 102(1-3). 108-115

Quality Enhancement Research Institute (2008). Substance use disorders. *QUERI Fact Sheets*. Washington D.C.: Department of Veterans Affairs

Reid, M., Angrist, B., Baker, S., Woo, C., Schwartz, M., Montgomery, A., et al. (2005a). A placebo-controlled screening trial of celecoxib for the treatment of cocaine dependence. *Addiction*, 100(1), 32-42.

Reid, M., Casadonte, P., Baker, S., Sanfilipo, M., Braunstein, D., Hitzemann, R., et al. (2005b). A placebo-controlled screening trial of olanzapine, valproate, and coenzyme Q10/L-carnitine for the treatment of cocaine dependence. *Addiction*, 100(1), 43-57.

Schmitz, J., Mooney, M., Moeller, F., Stotts, A., Green, C., & Grabowski, J. (2008). Levodopa pharmacotherapy for cocaine dependence: Choosing the optimal behavioral therapy platform. *Drug and Alcohol Dependence*, 94(1), 142-150.

Shoptaw, S., Majewska, M., Wilkins, J., Twitchell, G., Yang, X., & Ling, W. (2004). Participants receiving dehydroepiandrosterone during treatment for cocaine dependence show high rates of cocaine use in a placebo-controlled pilot study. *Experimental and Clinical Psychopharmacology*, 12(2), 126-135.

Shoptaw, S., Watson, D., Reiber, C., Rawson, R., Montgomery, M., Majewska, M., et al. (2005). Randomized controlled pilot trial of cabergoline, hydergine and levodopa/carbidopa: Los Angeles Cocaine Rapid Efficacy Screening Trial (CREST). *Addiction*, 100(1), 78-90.

Substance Abuse and Mental Health Services (2008). The national survey on drug use and health. *Inter-university Consortium for Political and Social Research*. Ann Arbor: United States Department of Health and Human Services

Thomas, M.J., Kalivas, P.W., Shaham, Y. (2008). Neuroplasticity in the mesolimbic dopamine system and cocaine addiction. *British Journal of Pharmacology*, 154(2). 327-42

Robyn Liebman

Winhusen, T., Somoza, E., Harrer, J., Mezinskis, J., Montgomery, M., Goldsmith, R., et al. (2005). A placebo-controlled screening trial of tiagabine, sertraline and donepezil as cocaine dependence treatments. *Addiction*, 100(1), 68-77.

Winhusen, T., Somoza, E., Sarid-Segal, O., Goldsmith, R., Harrer, J., Coleman, F., et al. (2007). A double-blind, placebo-controlled trial of reserpine for the treatment of cocaine dependence. *Drug and Alcohol Dependence*, 91(2), 205-212.