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Review Article

Improving Treatment of Alcoholism by Using Evidence-based Practices and Computer-assisted Game-like Programs

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Abstract

The idea is developed that computer-assisted game-like programs are a reasonable next step toward improving the treatment of alcoholism. Such programs are apt to be useful in rehabilitating the cognitive processes reduced by sustained intake of toxic amounts of ethanol and in counterconditioning the unconscious cues sustaining the habit of drinking alcoholic beverages. The evidence indicates that it is likely that prescribing naltrexone will facilitate psychotherapy for alcoholism, including practices useful in rehabilitating diminished cognitive ability.

Introduction

In many nations, a large proportion of adults and near-adults consume alcoholic beverages. Some consumers develop a strong habit of drinking intoxicating amounts. Habitual intake of intoxicating amounts is a substantial risk-factor for a number of severe health and social problems. When alcohol-related problems became apparent, the drinker might enter a treatment program, sometimes voluntarily, but often with coercion. The available treatments are usually, but not always, designed to help the drinker achieve and sustain abstinence.

There are positive and relevant outcomes other than complete abstinence [1]. Nevertheless, given the typical patient's expressed goals, the goals of their associates and most treatment programs, a reasonable metric for judging treatment-success is days abstinent for a period (say one year) after treatment, or during prolonged out-patient treatment. Another meaningful index of treatment-utility is number of drinks on any day of drinking with the goal of avoiding hazardous drinking. The stringent standard for success is a period of two years of abstinence, or very near abstinence, because such indexes further abstinence and fewer problems [2, 3].

Unfortunately, extant programs designed to achieve abstinence, or near abstinence, are only moderately successful. An obvious goal, therefore, is to improve them. No one expects every treated patient will become abstinent for years. Nevertheless, abstinence from intoxication remains the goal. Here, the idea is fostered that treatments can be improved with the introduction of computer-assisted game-like programs (CGPs) specifically designed (a) to rehabilitate the brain damage [4], manifest as reduced cognitive ability, induced by habitual intake of intoxicating amounts of alcohol and (b) reduce the impact of conditioned cues [5] eliciting the behaviors of habitually drinking alcoholic beverages. The use of CGPs is conceived to be an adjunct to evidence-based therapeutic procedures. In keeping with a modern perspective, it is recognized that an integrative, multidimensional approach involving evidenced-based psychotherapy having biological and sociological perspectives [see, 6, 7 for germane rationale] is necessary to achieve enhanced success rates in treating psychological disorders, including alcoholism.

Treatment of withdrawal signs and symptoms

The first step toward achieving long-term abstinence is managing withdrawal signs and symptoms. The prescription of a benzodiazepine is a treatment of choice to count-

er dangerous withdrawal [8,9]. Also, treatment with thiamine is often prescribed to counter Wernicke's syndrome [8,10]. Other nutritional interventions, such as attending to a potential zinc deficiency [11-14], might also improve treatment.

Delirium Tremens (DTs) is a serious manifestation of withdrawal. Prior to medical management, the death rate due to DTs was about 35%; but with medical management, it is currently only about 7 to 3% [15,16]. An extraordinary advance that may help manage DTs is the discovery that results from rather simple blood tests are very good at predicting whose withdrawal might advance to DTs [17].

During the days of withdrawal, particularly intense withdrawal, the patient is not in a favorable position to profit from education and psychosocial therapies. After the acute effects of withdrawal, some rest and good nutrition, treatment to prevent relapse begins.

Relapse prevention

Treatment providers use a variety of procedures to aid the newly abstinent patient to not relapse to pre-treatment levels of drinking. Many providers implement some version of a 12-step program (the Minnesota Model) involving a recommendation to affiliate with Alcoholics Anonymous (AA). There is usually some form of group therapy whose contents are varied in response to patients' concerns and the theory of alcoholism that guides the therapists' roles. Sometimes, a form of cognitive behavioral therapy is programmed [18-20].

Unfortunately, usual treatments designed to prevent relapse only achieve the goal for a modest proportion of those being treated [1,21-25]. What is interesting about attending to treatment-outcomes is that it seems to make only a little difference (a) what kind of psychosocial treatment was used; (b) whether the treatment was delivered by trained professionals or others; and (c) whether treatment was inpatient or outpatient, brief or prolonged [e.g., 26]. However, a few variables seem to be reliably associated with success-rates. Successful programs retain patients in the treatment-plan longer. Successful treatments have patients with features such as (a) a significant other looking after them (indexed by being married; having concerned parents; not living alone), (b) having a steady job or a history of such (or engaged in full-time education), and (c) being in treatment for the first time [27-29]. Less successful programs have patients without a significant other looking after them, with a history of unemployment and have been treated multiple times. Less successful treatments are with patients who are polydrug abusers and have an additional psychiatric diagnosis such as anxiety or depression [30, 31]. One can sum these variables by indexing the degree and duration of the intake of intoxicating levels of alcohol; those suffering the most toxicity are often the least likely to remain abstinent [32].

Engaging in a treatment program is better than not [33], even though the possibility exists that some of the constructs taught might be detrimental (e.g., "you have to hit bottom before you can recover," or a lack of optimism inherent to teaching that alcoholism is an incurable disease). Participation in one of the various programs of AA can add a small increment to rate of abstinence [34]. Nevertheless, treatments to prevent relapse typically do not work as well as they might as witnessed by this frequently given definition: alcoholism is a chronically relapsing disease [e.g., 22].

The prescription of naltrexone (Ntx) can improve success-rates. There is considerable preclinical data [e.g., 35-37] supporting the conclusion that prescribing an opioid antagonist would be a reasonable adjunct to extant treatments. Opioid antagonists, including Ntx, reduce laboratory animals' propensity to take large amounts of alcoholic beverages. Among humans, Ntx is a selective opioid antagonist whose oral doses block opioid receptors for 24 hours. Small doses of morphine, the classic opioid agonist, increased laboratory animals' usual intake of alcohol [36, 38]. A survey of college students' responses strongly supports the idea that taking opioid agonists promotes the use of alcoholic beverages [39].

The findings linking opioids to propensity to ingest alcoholic beverages followed considerable research showing that opioid antagonists reduced the rewarding aspects of a number of ingesta, particularly those usually taken with considerable avidity [40; for clear demonstration of such, see 41]. Collectively, these data support the idea that a portion of the endogenous opioid system is involved with sustaining the intake of palatable ingesta including alcoholic beverages. Patients attempting to reduce their intakes of large amounts alcoholic beverages, therefore, might profit from being dosed with Ntx.

Based on results of his own preclinical research, Joseph Volpicelli [42] and a colleague, Charles O'Brien, decided that sufficient data had accumulated to support a clinical trial of Ntx as an adjunct to ordinary treatments for, what was then termed, alcohol dependence. O'Brien, director of an addiction research center, had extensive experience using Ntx to treat prescription-opioid abuse [e.g., 43]. A well-designed clinical trial of a drug is expensive and time-consuming. In addition to these obvious constraints, when Volpicelli and O'Brien were contemplating a trial of Ntx, it is fair to say that there was general antipathy toward the idea that drugs, any drug, might be useful in treating alcoholism except to mute withdrawal or treat co-morbid conditions. These and related factors did not foster full financial support from industry or government. Nevertheless, and much to their credit, Volpicelli, O'Brien and their colleagues pulled together sufficient resources to engage a placebo-controlled, double-blind trial of Ntx.

At the half-way point in the planned procedures of Volpicelli et al., the blind was broken and the available results presented at a symposium. The symposium featured relevant preclinical research and the available clinical data on Ntx's effects on alcoholism [44] and on bulimia [45]. At the half-way point of Volpicelli et al.'s assessment, 30 patients with alcoholism had received Ntx and 30 others placebos. The Ntx-dose was (50 mg, taken daily, orally) sufficient to block most effects of abused opioids. There was a report that a 300 mg dose induced liver-damage [46]. Consequently, tests indicative of liver-damage were programmed. In brief, Ntx reduced the rate of relapse to problematic drinking. The controls' rate of relapse was very similar to rates usually obtained [21]. Further, the data indicated that those receiving Ntx had healthier livers than controls indicating that the Ntx-dose was safe, in terms of liver disease, even for those who might have minor liver-damage. News of the first trial prompted another. Reports of both Volpicelli et al.'s completed trial and the next trial appeared in 1992 [47, 48] (Figure 1). The USA FDA approved Ntx as treatment for alcohol dependence in 1994, their first new approval for alcoholism in roughly 50 years.

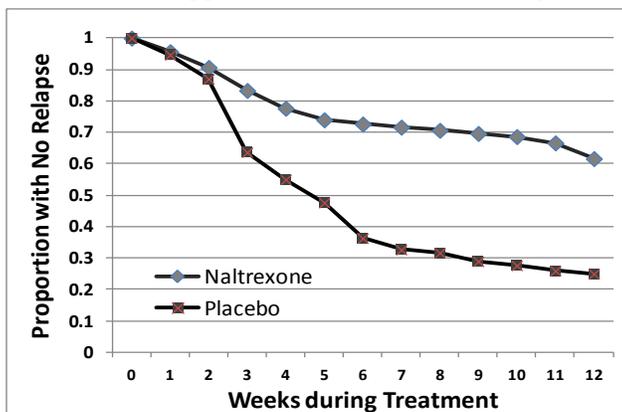


Figure 1. Depicted is my average of the results of the first two trials of Ntx, as an adjunct to treatment as usual, with respect to relapse rates [47, 48]. The rate of relapse among those receiving placebos is similar to the rate obtained by most treatment programs [21]. In general, relapse was defined as drinking toxic amounts of alcoholic beverages regularly.

There have been sufficient numbers of tests of Ntx-use as adjuncts to other treatments designed to prevent relapse to profitably do meta-analyses and systematic reviews [e.g., 49]. Rösner et al. [50] reviewed 50 studies (the number of well-done studies completed to 2010) with 7793 participants comparing the effects of oral doses of Ntx to placebos. The overall assessment: Ntx was moderately effective in treating alcoholism; providing substantial help to one of nine patients; although a seemingly small effect, better than placebo-treatment or treatment as usual. Ntx was deemed safe with minimal side-effects including some nausea with initial dosing [49, 50].

The limitations of Ntx were predictable from the preclinical research. Opioid antagonists reliably and substantially reduced intakes of alcohol, but as soon as the drugs were no longer given, intakes returned to pre-dosing levels [51]. With remarkable precision, small doses of morphine substantially increased intakes, and antagonists substantially decreased intakes, but these effects were not maintained beyond the days of dosing [52]. It is clear from extrapolation of the research using laboratory animals as well as findings derived from clinical trials that an advantage to prescribing Ntx is the provision of reduced intoxication providing a better opportunity for psychosocial therapy.

In trials assessing Ntx, compliance with the admonition to take Ntx daily was not followed by some patients [50, 53, 54]. A recent development designed to deal with the advice, or even a legal dictate, to take Ntx tablets daily is to prescribe an injection providing 28 days of circulating Ntx. The prescription to take injections providing extended release of Ntx (XR-Ntx) increases indices of success [55, 56]. The study of Garbutt et al. [55] was done with some patients who were not abstinent at the time of their first injections.

The pre-clinical data [52] lead to the conclusion that the endogenous opioid system is involved with sustaining intakes of rewarding ingesta once begun and that Ntx modulates this ordinary functionality. With respect to alcoholism, Ntx reduces incidents of toxic intakes, allowing for some healing (e.g., of liver, [44] and probably of brain). With well-established daily intakes of palatable alcoholic beverages, rats dosed with opioid antagonists invariably take some beverage, but stop taking it much sooner [57]. Among patients, a recent review [58] indicates that reduction in toxic amounts of alcoholic beverages is a benefit of Ntx, but indicates that Ntx does not stop sampling of alcoholic beverages sufficiently. There are, however, preclinical data [52] and clinical data [47,59] to indicate that opioid antagonists also mute the some of the secondary reinforcers having emerged by way of association with the primary reinforcement of drinking. Among patients, there is a reduction of craving [44,47] which may be a manifestation of reduction of the salience of secondary reinforcing cues [60].

Although there are other drugs (e.g., acamprosate, baclofen, ondansetron and topiramate) that can be used as adjuncts to usual treatments [56, 61, 62], the advice is to use Ntx because it will be useful in treating common co-morbid disorders including binge eating and bulimia nervosa [63] as well as other "out-of-control" behaviors such as gambling [64]. Ntx will block abused opioids' effects [65]. Some procedures might enhance the effectiveness of Ntx; for example, tailoring the dose to the patient's size and the seriousness of the alcoholism. Also, it seems that therapists might strongly urge the use of Ntx with groups of patients for which there

are some data to indicate that Ntx is particularly useful [66].

As might be expected given the fact that opioid receptors are extensive and widely distributed [67], Ntx has extensive effects, only some of which might be critical to treating alcoholism. Some of these effects limit the use of Ntx with women who are pregnant or apt to become pregnant [68]. Despite the well-supported conclusion that Ntx is remarkably safe and that some individuals have sustained the state induced by Ntx for years without obvious ill effects, the idea of blocking the ordinary functions of an extensive system of brain and body for an extensive period surely has many effects in addition to those helpful in treating alcoholism and attendant problems. Many of those potential long-term effects have not been studied in detail (e.g., increased risk of depression, modulation of cell proliferation [69], changes in sexual functioning [70]) making it risky to prescribe Ntx for extensive periods. Given the inevitable limitations of knowledge about long-term effects, it seems prudent to limit the prescription of any psychotropic drug for the treatment of alcoholism. Therefore, the recommendation is to use Ntx as a setting condition for psychotherapy with the understanding that psychotherapy, in some form, may involve a considerable period, extending for months. Further, it is reasonable to presume that the withdrawal from Ntx might be a particularly difficult time for a recovering alcoholic and, therefore, it will be optimal to plan therapy for such a transition.

Recent research has confirmed that injections providing nearly month-long moderate doses of Ntx do enhance the rate of achieving abstinence or near abstinence among those formally diagnosed with alcoholism [66]. Although some patients do opt out of taking more than a couple of injections, some patients voluntarily take multiple injections and in so doing achieve a reduced rate of taking toxic amounts of alcoholic beverages [66, 71]. One study [72] involved treatment of 31 homeless people with alcoholism who took advantage of the opportunity to take XR-Ntx once each month for 3 months. There were measures of extent of drinking, a tabulation of problems, and indices of liver-health. Twenty-four of the 31 who received the first injection of XR-Ntx completed all procedures. The results of this pilot study were encouraging; the homeless alcoholics reported less drinking, experienced fewer problems, and better liver-health compared to their measures prior to participation in the procedures. As with oral dosing, a salient advantage to XR-Ntx dosing is an enhanced opportunity to engage evidence-based psychosocial therapies such as cognitive behavioral therapy and help toward developing healthy life-styles.

Managing withdrawal signs and symptoms, programming good nutrition and other healthy practices (e.g., exercise), beginning to correct the problems that have accrued as a result of alcoholism (e.g., chronic unemployment, not attending to social and legal obligations), cognitive therapy to change irrational beliefs, urging attendance at AA meetings compatible

with the patients' beliefs, and the time-limited prescription of Ntx (preferably XR-Ntx) are steps toward recovery from alcoholism. Research supports the salience of each of these separately and the combination of many of them [18, 73]. There is the strong, but mostly untested, conviction that the combination of these steps will surely help many to develop a life-style supporting sustained abstinence. However, it is highly likely that many persons suffering alcoholism will attempt the goal of prolonged abstinence or near abstinence with an ethanol-induced reduction of cognitive ability, a salient handicap.

Cognitive Rehabilitation

Habitual intake of intoxicating amounts of alcohol is, indeed, toxic to brain as manifest by measures of cognitive functioning and studies of the brain's anatomy. Oscar Parsons spent decades studying the possibility of neurocognitive deficits in abstinent alcoholics. He summarized: "... both male and female adult alcoholics--compared with peer nonalcoholic controls--have deficits on tests of learning, memory, abstracting, problem-solving, perceptual analysis and synthesis, speed of information processing, and efficiency. The deficits are equivalent to those found in patients with known brain dysfunction of a mild to moderate nature. Attempts to identify factors other than alcoholism to account for these differences have been unsuccessful. The deficits appear to remit slowly over 4 to 5 years. ... Results of recent studies support the hypothesis of a continuum of neurocognitive deficits ranging from the severe deficits found in Korsakoff patients to moderate deficits found in alcoholics and moderate to mild deficits in heavy social drinkers (more than 21 drinks/week)" [4, p 954]. More recent research has shown that these deficits are manifestations of considerable anatomical change in both brain's grey and white matter [74-78].

George Koob [79, 80] has posited that what eventually happens to the habitual drinker of intoxicating amounts of alcohol is a rather abrupt change in brain that accounts for the apparent irrationality of continuing to drink alcoholic beverages when it doesn't, according to theory, produce much, if any, pleasure and produces misery. This change has been described as a persistent or near-permanent (e.g., epigenetic) neuroadaptation manifest as "loss-of-control." The procedure supposedly modeling this neuroadaptation is forcing laboratory-animals, usually rats, to breathe ethanol-vapors for hours, periodically, which induces marked withdrawal signs. Following dosing with ethanol-vapors, animals regularly increase voluntary intakes of alcoholic beverage. It also produces indices of allosteric load, e.g., hypercortisolemia.

It may be unnecessary to posit any special epigenetic neuroadaptation to account for loss-of-control. The cumulative toxic effects of large doses of ethanol, as manifest by tests of cognitive ability, may be sufficient. Ethanol's toxicity is

prominently displayed in areas of the brain salient to executive processes [76, 81]. Executive processes are necessary for changing the thrust of behavior once begun and, in a broader sense, for the newly abstinent alcoholic to make the necessary changes in life-style. Executive processes are also critical to impulse control (resisting temptation) [82]. Regardless of whether the damage due to ethanol's ability to disrupt salient structures of brain is sufficient to account for loss-of-control, it is desirable that the effects of ethanol's toxicity be ameliorated with the beginning of abstinence so that the patient has the ability to make changes sustaining abstinence or near abstinence.

Decades ago, the prevailing theory was that once a brain was damaged (neurons destroyed or seriously debilitated), it was damaged forever and that there was no neurogenesis in adults' brains. Accordantly, the only recourse for a person with brain damage was to learn to cope with a handicap. Modern theory is different. In the most general sense, it is now understood that the constant incoming sensory information associated with a working nervous system molds the functionality of the brain including even shaping the anatomy of the forebrain as the individual copes with inevitable changes in circumstances. It is now understood that neurogenesis is possible and probably can continue throughout the lifespan. This new perspective has labels: Brain plasticity or neuroplasticity, in recognition that even in the adult brain there can be an epiphenomenon of significance, manifest at a gross anatomical level, which emerges from processes of multiple, but systematic, changes at the synaptic level. The brain plasticity movement is well-chronicled in a number of recently released books [83-85]. Of note: the term plasticity is also used to connote [e.g., 86] the more ordinary processes of habit formation (Hebbian learning manifest in processes studied by Pavlov and other early learning theorists).

An implication of the brain plasticity perspective: Perhaps, if we tried, we could rehabilitate an ethanol-damaged brain; we could restore it to its pre-damaged state; and even optimistically improve its functionality. Except in cases of the most severe damage (e.g., Korsakoff's syndrome), and without any specific intervention, there is usually slow recovery of cognitive abilities [4, 81] provided, of course, there is abstinence or near abstinence (and, interestingly, no smoking of nicotinic cigarettes [87]). Perhaps, with specific intervention, cognitive processes can be improved faster and, thereby, institute an enhanced ability to adopt an abstinent life-style.

New theory indicates that the anatomy of a damaged brain can be changed for the better; nevertheless, it is clear that such does not happen without many hours of specialized practice. The commercial success of recreational video games indicates the games can sustain prolonged practice. Theoretically, features of the gaming technology can be programmed to engage the sustained practice necessary for cognitive rehabili-

tation. The issue, of course, is what kind of practice will, indeed, rehabilitate the lost abilities and strengthen abilities to control impulses and change habits (necessary outcomes for sustaining abstinence which, in turn, will foster further recovery).

Executive functioning is a theoretical construct designed to index abilities to plan, to resist temptation, and to work for delayed rewards. Most theorists indicate that a well-developed working memory is integral to successful executive functioning; consequently, tests for executive functioning often includes tests of working memory. There are a number of psychometrically sound tests to index degree of executive functioning. Many of them can be administered with the aid of a computer. The idea is to take the various tests indexing executive functioning and use them as prototypes to develop computer-assisted game-like programs (CGPs) that encourage practice at the tests' intellectual tasks. In brief, as an effort to enhance executive functioning, have persons with alcoholism practice, in a game-like context, the very tests that are usually used to measure executive functioning. There is no controversy about whether, if you can get a person to practice the features of a particular test for executive functioning, that performance on that test can be increased considerably; the more practice the greater the gain in performance. A controversial issue is whether such improved performance will increase ability to function in day-to-day life (i.e., enhance intelligence) [88]. There are data to support the idea that practicing intellectual skills does go some way toward cognitive rehabilitation of injured brains beyond merely teaching victims to cope with their injury [85, 89].

If the goal of treatment for alcoholism is to change well-established habits from those sustaining drinking to those that are healthier; if most alcoholics entering treatment have reduced cognitive ability; if it takes considerable intellectual flexibility and strength to change well-established habits; and if cognitive rehabilitation is a possibility, then it follows that one is apt to agree with Bates et al. [90, 91] that treatment for alcoholism should focus on cognitive rehabilitation. The issue becomes how to provide the means for cognitive rehabilitation. The possibility is that CGPs specifically designed to (a) to rehabilitate ethanol-induced brain damage and (b) reduce the impact of conditioned cues eliciting the behaviors of habitually drinking alcoholic beverages will add considerably to the effectiveness of alcoholism treatment [86].

The brain state induced by Ntx is likely to be compatible with cognitive rehabilitation [92, 93]. Crews and Boettiger [94] have findings indicating that Ntx increases activity in the frontal cortical areas and such activity is apt to facilitate the processes inherent to the goals of CGP training [60]. Ntx has another feature that may not seem beneficial at first. A drug completely suppressing the urge to drink with its initial introduction is apt to be less than useful because such a drug would have ubiquitous effects. Drugs impairing learning or

near critical physiological processes are antithetical to establishing new life-styles sustaining sobriety. To countercondition the unconscious cues directing any well-established habit, including those of alcoholism, it will be necessary to have features of those cues present in order to replace them with new associations as demonstrated by the successful treatments for phobia and other anxiety disorders [6, 95, 96]. The optimal drug is one that reduces the compulsivity of a problematic habit thereby making treatment more likely, but not totally suppress features of the habit and Ntx meets that criterion.

Fals-Stewart and Lam [97], Houben et al. [98] and Rupp et al. [99] have each assessed the value of training for improved executive functioning on propensity to drink intoxicating amounts of alcohol. Each study supported the conclusion that such training would enhance treatment-outcomes. I posit that making the training more focused on circumstances more salient to alcoholism would result in even further enhancement of treatments.

Two examples of how one might develop specific alcohol-related CGPs as supplements to treatment as usual are summarized: (a) a go/no-go task which when practiced with alcohol-related symbols has been shown to reduce salience of cues related to alcohol-use [100] and (b) a shopping game with features similar to the trail making test. The results of the trail making test reliably measures extent of brain damage [101].

The go/no-go procedures of Kreuzsch et al. [100] used symbols characteristic of alcoholic beverages and brand logos. The result was a reduction in an automatic, unconscious response to alcohol cues and one may reasonably conclude that an extension of such practice might further the goal of abstinence once obtained. It might be more productive to use words such as rum, whiskey, martini, wine, beer, ale, etc. as no-go signals and other words as go signals. Using words, it is posited, has more cognitive connotations than symbols. The "game" would start at an easy speed of presentation of either graphic symbols or words and only progress with clear signs of success (withholding a response to alcohol-related cues) before introducing quicker presentation-rates. Successful responses would be accompanied by a sign of success. The accumulation of successful no-go responses would be praised periodically.

Laloyaux et al. [102] have developed a simulated grocery-shopping task for the computer as a test of cognitive ability and its use separated those with a history of alcoholism from non-drinking controls. The test's results were positively correlated with other indices of success at completing day-to-day chores. Laloyaux et al. [102] also indicated that the task was correlated with other tests of executive functioning including those specifically measuring cognitive flexibility, planning and inhibition; abilities Noël et al. [103] found to be salient predictors of relapse (also [77]). They also indicated that a shopping test would probably be a good proxy for other chores of everyday life. Interestingly, time to complete the shopping task was a

strong indicator of overall performance just as time to complete the trail making test is the useful measure [101], a likely outcome since the two tests are similar. The shopping task can be tailored to develop a CGP that, with practice, will enhance the ability to do the program as it progresses from the very simple task of getting a small number of items from a simulated store as quickly as possible to getting many items as quickly as possible. To sustain practice, features of successful video games can be used including consistent delivering of praise, creating a narrative to accompany the task, and providing a consistently challenging task that one is likely to succeed at accomplishing.

Notice that some of the controversy associated with the issue of does practice at the tests of executive functioning transfer to day-to-day functioning (i.e., actually increase intelligence) is obviated to some extent by making the games (a) particularly salient to alcohol related variables (e.g., the proposed go/no-go task) and (b) particularly relevant to improved day-to-day functioning (e.g., the proposed shopping game). Well-designed CGPs specific to alcoholism may not increase overall intelligence, but will likely increase "intelligence" with respect to habitually drinking toxic amounts of alcohol.

Of course, CGPs can vary considerably from ones poorly conceived and poorly done to better ones. With an enhanced interest in developing CGPs for use in the treatment of alcoholism, surely, some CGPs will be designed cleverly and sustain practice whereas others will be boring. Given the possibilities for variance in CGPs, it will be easy to demonstrate that CGPs are ineffective (provide an irrelevant, boring game to a group of newly abstinent alcoholics and they surely will not practice it sufficiently to be helpful). Given this circumstance, it will be necessary to provide adequate resources for multiple teams to develop CGPs that developers believe will be effective and then keep tabulations allowing judgments of effectiveness. With feedback on potential success, the games can be continually improved. Unlike some interventions, modern technology allows for continuing feedback on use of a well-developed CGP. A relatively simple measure of potential utility of any given CGP as a feature of treatment for alcoholism would be the extent of time the game was played. Aside from the possibility that CGPs are apt to beneficially add to treatment as usual, they would be a cost-effective way of improving treatments that can even be done at home, at virtually anytime and with little professional intervention.

There is research supporting the use of Ntx, providing cognitive behavioral therapy, and attempting cognitive rehabilitation as ways to improve the usual treatment of alcoholism. Further, there are indications that the combination of Ntx and cognitive behavioral therapy is better than either alone [18]. Unfortunately, many treatment programs have yet to incorporate these likely improvements and, hence, fail to achieve enhanced rates of changed life-styles supporting prolonged

abstinence. It is clear, habitual intake of intoxicating amounts of alcoholic beverages reduces the functionality of the brain and such damage is manifest in reduced cognitive ability hindering the learning of new habits that will sustain sobriety. Although initial indications are the CGPs are apt to facilitate treatments, there is only limited work toward using germane modern technology to improve treatment of alcoholism.

What has been outlined here is a rather commonsensical approach to treating alcoholism and the suggestions for improving treatments are rather straightforward extensions of the available research. Despite the reasonable expectation that implementing these evidence-based practices would improve treatment, there are indications that "treatment as usual" has not been updated in concordance with the available research. For example, research circa 2008-2009 indicated that less than 4% of patients being treated for alcoholism in the USA's Veterans Administration health care system are prescribed medications to help prevent relapse and the use of some of the prescribed drugs are not supported by the available evidence [104]. At some facilities, no patients were prescribed Ntx. According to some accountings, the prescription to take Ntx (orally at the low dose of 50 mg/person/day) would probably be benefiting to as many as 8% [104] or 11% [50] more patients than benefitted from treatment as usual. More are apt to be helped by larger doses of Ntx and XR-Ntx. Given that as many 331,635 veterans are undergoing treatment for alcohol use disorder (data circa 2009) [104], the use of NTX could conservatively benefit somewhat more than 25,000 veterans attempting to change life styles to one that does not involve habitual intake of alcoholic beverages. Those not being helped substantially by widespread use of Ntx will have very few adverse side-effects provided that Ntx dosing is limited to months and may even facilitate advanced psychotherapy (such as evidenced-based cognitive behavioral therapy and CGPs). It terms of proportion of patients that might be helped by therapies supported by evidence, the wins are modest. In terms of the number of patients that will benefit, the wins are extensive. Further, there are indications that XR-Ntx therapy reduced costs for medical care [105-107]. Perhaps, if all was taken into account, it is possible that the health care system is already spending excessively in comparison to what might be spent by practicing evidence-based treatment for alcohol use disorders.

What can account for any system's resistance to practicing evidence-based therapy, particularly when the evidence indicates such is likely to be more effective, safer and less costly than the alternatives? It is difficult to account for the resistance; however, it should be noted that there are extensive vested interests in sustaining the way things are now, including those of the alcohol beverage industries. If treatment to prevent relapse were dramatically improved, the alcohol beverage industries would lose their best customers; for example, among those who drink, the heaviest drinkers (heaviest 5%) buy about 40% of the

total volume drunk and account for about 24% of dollars spent on alcoholic beverages [108]. If a national system charged with treating alcoholism regularly helped even half of the heaviest drinkers to be abstinent or near abstinent, the alcohol beverage industries would suffer, but it would be in a good cause.

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