Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplemental Appendix

Neurobiological Advances from the Brain Disease Model of Addiction

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Supplemental BOX S1. Criticisms of the Brain Disease Model of Addiction[1] and Counter-Arguments

1. **Most people with addiction recover without treatment, which is hard to reconcile with the concept of addiction as a chronic disease**. This reflects the fact that the severity of addiction varies, which is clinically significant for it will determine the type and intensity of the intervention. Individuals with a mild to moderate substance use disorder, which corresponds to the majority of cases, might benefit from a brief intervention or recover without treatment whereas most individuals with a severe disorder will require specialized treatment[2].

2. **Addicted individuals respond to small financial rewards or incentives (contingency management), which is hard to reconcile with the notion that there is loss of control in addiction**. As described here, some of the behavioral abnormalities associated with addiction follow from the learned or conditioned pairing of situational cues with the powerful incentives of the drug effects. The demonstrated effectiveness of contingency management shows that financial cues and incentives can compete with drug-cues and incentives – especially when those financial incentives are significant and relatively immediate [3,4]; and when control has been simply eroded rather than lost. Contingency management is increasingly being utilized in the management of other medical disorders to incentivize behavioral changes (i.e., compliance with medications, diets, physical activity).

3. Gene alleles associated with addiction only weakly predict risk for addiction, which is hard to reconcile with the importance of genetic vulnerabilities in the Brain Disease Model of Addiction. This phenomenon is typical of complex medical diseases with high heritability rates for which risk alleles predict only a very small percentage of variance in contrast to a much greater influence of environmental factors (i.e., cirrhosis, diabetes, asthma, cardiovascular disease)[5]. This reflects, among other things, that the risk alleles mediate the response to the environment; in the case of addiction, the exposures to

drugs and stressful environments [6].

4. Overlaps in brain abnormalities between people with addiction and control groups, raises questions on the role that brain abnormalities have on addiction. The overlap is likely to reflect the limitation of currently available brain imaging techniques (spatial and temporal resolutions, chemical sensitivity), our limited understanding of how the human brain works, the complexity of the neurobiological changes triggered by drugs and the heterogeneity of substance use disorders.

5. Treatment benefits associated with the Brain Disease Model of Addiction have not materialized. Medications are among the most effective interventions for substance use disorders for which they are available (nicotine, alcohol and opiates). Moreover, progress in the approval of new medications for substance use disorders has been slowed by the reluctance of pharmaceutical companies to invest in drug development for addiction.

6. **The Brain Disease Model of Addiction neglects public health policies in favor of biomedical treatments**. This is questioned on the basis of dollars spent by the National Institute of Drug Abuse (NIDA) and the National Institute of Alcohol Abuse and Alcoholism (NIAAA) on research on public health versus biomedical treatments. However, the issue is not the need for more research on public health policies since many already exist but rather for their implementation. On the other hand, there are few biomedical treatments currently available for substance use disorders and so this area remains a priority

7. Benefits to policy have been minimal. The Brain Disease Model of Addiction created the foundations for the Patient Protection and Affordable Care Act and provision of health-care through Obamacare [7]. Thus the Brain Disease Model of Addiction provided the basis for patients to be able to receive treatment for their addiction and for

insurances to cover for it. This is a monumental advance in health policy. The Brain Disease Model of Addiction also provides key evidence –based science for retaining the drinking age at 21 years.

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Supplemental BOX S2. Behavioral addictions

The concept of behavioral addictions has been controversial particularly as it relates to the concept of "food addiction" and its contribution to obesity [1]. However, there is increasing recognition that the rewarding effects of food, particularly food rich in fat and sugar, can trigger neuroadaptations in the brain reward and stress circuitry that are similar to those produced by addictive drugs [2]. Interestingly, peripheral signals involved in satiety and hunger (i.e., leptin, insulin, ghrelin) that influence the sensitivity of the brain dopamine system to the rewarding effects of food also modulate the sensitivity to the rewarding effects of various drugs [3]. Studies have also identified significant overlaps (though also unique differences) among the brain circuits affected in addiction and obesity [4]. Similarly, it is interesting that cues repeatedly associated with fat/sugar rich foods (e.g., TV commercials) also appear to acquire the power to produce exaggerated reactivity (craving) and reduced control over food intake; as well as increased negative emotional reactivity when attempting to refrain from eating [5]. Pharmacological studies have also shown that medications used in the treatment of addiction (naltrexone/bupropion) can be beneficial for the treatment of obesity [6] and medications for obesity may hold promise for addictions (lorcaserin)[7]. Similarly, behavioral interventions beneficial in the treatment of addiction have shown benefit in the treatment of obesity [8]. The current consensus is that only a subset of individuals with obesity (those with a binge-eating disorder) suffers from "food addiction". However, the *DSM–5*, does not include binge-eating disorder among the addictive disorders. Internet gaming is the only non-substance based disorder considered by DSM-5 as an addictive disorder.

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