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# Too much of a good thing: Neurobiology of non-homeostatic eating and drug abuse

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#### Abstract

In this paper, a framework involving four aspects to be considered when establishing an operational definition of non-homeostatic appetitive behavior is presented. The four aspects are (1) the quantity of the commodity consumed, (2) the quality or type of commodity consumed, (3) the context in which the behavior occurs, and (4) the specific kind of behavior that is directed toward obtaining and consuming the commodity of interest. This framework permits comparisons among a variety of non-homeostatic behaviors and accommodates different theoretical approaches reflected in the use of mechanistic, systems, behavioral, nutritional, and clinical experimental strategies. The speakers of this symposium were selected to emphasize the four aspects of non-homeostatic behavior, to represent several different approaches, and to facilitate discussion regarding neural similarities and differences between non-homeostatic eating and drug abuse. The various talks illustrated that boundaries need not exist among research fields, and that communication among the various areas enhances the research effort.

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#### 1. Definition of non-homeostatic appetitive behavior

The first requirement of any informed discussion of non-homeostatic behavior is to clearly define what that behavior is. We have identified four aspects that we believe are important to consider in an operational definition of non-homeostatic appetitive behavior. These are: 1) the quantity of the commodity consumed, 2) the quality or type of commodity consumed, 3) the context in which the behavior occurs, and 4) the specific kind of behavior that is directed toward obtaining and consuming the commodity of interest.

#### 2. The factor of quantity

Non-homeostatic behaviors usually involve engaging in a certain behavior to an excessive amount, for instance gambling compulsively or drinking excessive amounts of alcohol. Non-homeostatic eating, on the other hand, involves consuming too much or too little food relative to what is biologically required (i.e. defined by homeostatic needs). It is quite normal, of course, to overeat on some occasions and to undereat on others. It is regarded "normal" not only because of the consensus of our society [1], but also because homeostatic regulatory mechanisms for the short-term, and adaptive regulation for the long-term, compensate for deficits and excesses within a certain regulatory range [2]. We have elected to call such events "compensated" non-homeostatic eating. However, when overeating or undereating occurs repetitively or excessively, mental and/or physical health can become compromised, i.e. the behavior ceases to be "normal" and becomes "maladaptive" or "dysfunctional." We have elected to use the term "maladaptive" because it refers to the failure to adapt appropriately. Adaptability is an essential feature of consumatory behavior that increases the chance of survival of the organism/individual. Excessive intake - in either

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direction —becomes maladaptive when it shortens life expectancy or increases the risk of disease. "Maladaptive" overeating promotes the development of obesity, while "maladaptive" undereating characterizes the eating disorder anorexia nervosa. Recent evidence suggests that neural mechanisms associated with obesity [3] and anorexia nervosa among human subjects [4] may overlap with mechanisms associated with substance abuse.

#### 3. Quality also matters

The aspect of quality refers to the type of commodity toward which behavior is directed. In the case of drug abuse, quality would refer to the type of drug consumed, e.g. alcohol, cocaine, heroin, etc. Non-homeostatic eating involves consuming specific foods or nutrients in quantities that do not promote health (i.e., disproportional to need). Much research has focused on understanding the neurobiology involved in the overconsumption of fat and sugar [5–9]. Conversely, consuming insufficient quantities of certain foods and/or nutrients can certainly be non-homeostatic, as the many nutritional deficiency diseases demonstrate. However, even without inducing a nutrient deficiency, underconsumption of certain foods and/or nutrients may still be considered non-homeostatic. For instance, recent studies suggest that diets containing lower amounts of calcium and/ or low-fat dairy products can contribute to increased body weight [10].

#### 4. Why is context so important?

The context in which behavior occurs can contribute to the maintenance of that behavior through classical and/or operant conditioning. That is, once a stimulus gains behavioral relevance, it becomes a cue or stimulus that, in turn, can promote the repeated occurrence of the behavior. For this reason, the context in which behavior occurs is important to consider when defining any behavior as nonhomeostatic. Occasionally eating during the night, for instance, is normal; repeatedly eating at night becomes maladaptive [11]. Animal research relevant to context has shown that access conditions can differentially affect cocaine's reinforcing efficacy as well as the amount of food consumed [12,13]. Furthermore, contextual cues associated with addictive drugs and palatable foods cause similar patterns of early gene expression in the prefrontal cortex [14]. Other recent work used a protocol in which brief 20-min daily access to sucrose was provided in a context of time cues as well as following chow availability in restricted-fed rats. Under these conditions, dopaminergic alterations occurred after as few as six days that were not apparent in control rats that had equal access to sucrose but received it outside of the context or without food restriction [15-17]. Such studies may be useful for studying snacking behavior or the neurochemical plasticity in restricting bulimics.

These reports indicate that something more than simply the preference for certain foods (i.e. systems involved in "liking") is required for development of neural plasticity that is similar to the effect of drugs of abuse (i.e. systems involved in learning and "wanting") [18]. Many have examined neural similarities (see for example Refs. [6-9,19]) and differences between the responses to food and drugs of abuse (see for example [20-22]). Whether discussing similarities or differences, it is clear that conditioned incentives attached to both drug- and foodrelated cues are important in modulating behavior directed toward obtaining and consuming both commodities. Such conditioning serves as a model for the contribution of environmental context to the maintenance of non-homeostatic behavior, and is thought to be critical to relapse [23,24].

### 5. Disordered behavioral patterns are characteristic of non-homeostatic behavior

Finally, the specific expression of the behavior itself is important to consider. In non-homeostatic eating, meal-size and appetite need to be studied separately from the overall amount consumed. Even if overall energy intake is in equilibrium with expenditure, consuming that amount of food rapidly in a brief period of time (bingeing) would certainly challenge physiological equilibrium. Everyone binges occasionally, which is normal. However, when bingeing occurs repeatedly over extended periods of time it becomes maladaptive, since neither the capacity nor the clearance and feedback mechanisms of our alimentary and central regulatory systems were designed for such an overload [25,26].

Disordered eating patterns can involve undereating or overeating, as well as combinations of both. For instance, inappropriate self restriction is a compensatory behavior used by many bulimics, whereas bingeing is characteristic of the binge/purge type of anorexia nervosa. Whether these combinations reflect homeostatic compensatory attempts or rather are part of the pathophysiology of the disorders (e.g. opponent-processes theory, [27]) is not known. Nonetheless, the fact that maladaptive patterns are maintained in spite of the negative consequences associated with them characterizes many of the behavioral disorders, including substance abuse and disordered eating.

#### 6. Potential approaches to the study of maladaptive nonhomeostatic eating

In summary, we are characterizing non-homeostatic appetitive behavior based upon the *quantity* and *quality* of the commodity consumed, the *context* in which the behavior

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