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Bingeing rats: A model of intermittent excessive behavior?

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Abstract

Intermittent excessive behaviors (IEB) characterize a variety human disorders including binge eating, drug abuse, alcoholism, aberrant sexual conduct, and compulsive gambling. Clinical co-morbidity exists among IEB, and limited treatment options are available. The use of behavioral models of bingeing and other feeding protocols is beginning to clarify neural similarities and differences that exist between IEB directed toward obtaining and consuming food and IEB directed toward obtaining and consuming drugs of abuse. Research from this laboratory using a limited access binge-type eating protocol may provide new insight into IEB.

Keywords

Binge eating; Substance abuse; Behavioral models

What are intermittent, excessive behaviors?

Intermittent excessive behaviors (IEB) characterize a variety human disorders including binge eating, drug abuse, alcoholism, aberrant sexual conduct, and compulsive gambling. These behaviors are associated with increased morbidity and mortality, but are maintained in spite of the negative consequences associated with them. Over the past few decades, increased attention has been given to understanding the neurobiological basis of intermittent episodes of behavioral excess, with particular effort focused on reducing drug abuse and the overconsumption of food. The hope is that elucidation of the neurobiological underpinnings of one type of behavior (e.g. feeding) will enhance our understanding of other types of behavior (e.g. drug abuse). This would provide a basis for the development of new therapeutic interventions that could be effective in a variety of disorders. Although, recent reports indicate progress in the pharmacological treatment of disorders involving bingeing and certain addictions, treatment options remain limited and relapse rates are high (de Lima, Soares, Reisser, & Farrelle, 2002; Halmi, Agras, Mitchell, Wilson, Crow and Bryson, 2002; Kreek, LaForge, & Butelman, 2002; Safer, Lively, Telch, & Agras, 2002; Zhu & Walsh, 2002).

In humans, IEB directed toward consuming food is perhaps best represented by binge eating. Binge eating involves the intermittent overconsumption of food in brief periods of time in an amount that is more than most individuals would eat under similar circumstances. The binge may or may not be followed by compensatory behaviors such as vomiting ('purging'), fasting, or excessive exercise. In the bingeing-related eating disorders, binges occur frequently over long periods of time and are associated with a sense of loss of control and emotional distress (DSM-IV, 1994).

Binge eating shares comorbidity with other IEB. For instance, patients seeking treatment for alcohol and cocaine abuse experience high rates of binge eating (Johnson, Spitzer, Williams,

Kroenke, Linzer and Brody, 1997; Wilson, 1993), and populations seeking treatment for bingeing-related eating disorders experience high rates of substance abuse, particularly of alcohol and cocaine (Brewerton, Lydiard, Herzog, Brotman, O'Neill and Ballenger, 1995; Bulik, Sullivan, & Kendler, 2002; Bushnell et al., 1994; Herzog et al., 1992; Laessle, Wittchen, Fichter, & Pirke, 1989; Wiederman & Pryor, 1996). A relationship between binge eating and gambling has also been reported (Engwall, Hunter, & Steinberg, 2004).

The comorbidity among IEB suggests that mechanisms mediating these behaviors may overlap. Animal models are needed to examine alterations that occur during IEB development, maintenance, and relapse, and to compare similarities and differences between different IEB classes. Protocols utilizing natural rewards such as food are of particular interest because of their ability to reveal changes that occur when occasional normal behavioral excess (e.g. occasionally bingeing) is transformed into repetitive, intermittent, maladaptive behavioral excess (e.g. repeatedly bingeing). Several behavioral models of binge-type eating have been proposed, which recently have been reviewed (Corwin & Buda-Levin, 2004). The use of these and other protocols is beginning to clarify neural similarities and differences that exist between IEB directed toward food and IEB directed toward drugs of abuse (for example, Bello, Sweigart, Lakoski, Norgren, & Hajnal, 2003; DeSousa, Bush, & Vaccarino, 2000; Di Chiara, 2002; Gosnell, 2000; Grigson, 2002; Hagan & Moss, 1991; Kelley & Berridge, 2002; Schroeder, Binzak, & Kelley, 2001; Spangler, Wittkowski, Goddard, Avena, Hoebel and Leibowitz, 2004).

Bingeing rats and IEB

The limited access protocol

Research from this laboratory has been directed toward developing a behavioral model of binge-type eating that does not require energy restriction, in order to minimize potential confounds associated with food-deprivation. Therefore, a nutritionally complete laboratory chow and water are provided at all times in our protocol. To induce binge-type eating, limited access to an optional source of dietary fat (hydrogenated vegetable shortening) is provided. Our research has shown that, as access to the shortening decreases, consumption of the shortening increases during the 2-h limited access period (Corwin, 2004; Corwin, Wojnicki, Fisher, Dimitriou, Rice and Young, 1998; Dimitriou, Rice, & Corwin, 2000; Thomas, Rice, Weinstock, & Corwin, 2002). When rats only have access to the shortening for 2 h three times a week, intake during the 2-h access period is very high, i.e. equivalent to what rats with continuous access to shortening consume in 24 h. Establishing these elevated intakes takes about 4 weeks. However, once established, the behavior is easily maintained. This protocol provides a relatively simple and inexpensive means of establishing IEB that can be maintained for extended periods of time. The phenomenon is robust and reliable, as we have demonstrated it in different strains and ages of rats (Thomas et al., 2002), as well as in males and females (Corwin et al., 1998; Dimitriou et al., 2000).

Rats with access to shortening for 2 h on Mon, Weds, Fri (MWF) each week do not compensate for the excess energy consumed during the binge in the 22 h following the binge episode. That is, the excessive intake during the 2-h binge causes significant 24-h overconsumption on the binge day. On subsequent non-binge days, however, 24-h energy intake is reduced. Thus, a binge/compensate behavior pattern develops in the MWF rats, even though they are never deprived of food; only their access to the shortening is limited. The pattern of food intake in the MWF rats is different from that of rats maintained on the daily 2-h shortening access schedule. Daily 24-h food intake in those rats does not differ from chow-only controls on most days.

The fact that bingeing in the limited access protocol is induced by limiting access to a preferred high-fat food is relevant, because binge foods consumed by humans typically consist of restricted 'forbidden' high-fat items such as snacks and desserts (DSM-IV; Guertin, 1999; Hadigan, Kissileff, & Walsh, 1989; Kales, 1990; Rosen, Leitenberg, Gross, & Willmuth, 1986). In addition, limiting access to snack foods increases their subsequent consumption in a controlled laboratory setting (Fisher & Birch, 1999). The fact that rats on the limited access protocol are not food-deprived is also relevant, as eating in the absence of hunger has been associated with bingeing in humans (Marcus & Kalarchian, 2003). The behavior of animals on the limited access protocol, then, has relevance to human food intake, and is similar in some ways to that of humans suffering from bingeing-related eating disorders.

Peptides that regulate fat intake are without effect under limited access conditions

In non-binge protocols, galanin stimulates fatty food intake when administered directly into the paraventricular nucleus of the hypothalamus (Corwin, Robinson, & Crawley, 1993; Kyrkouli, Stanley, Seirafi, & Leibowitz, 1990), and the galanin antagonist M40 reduces fat intake (Leibowitz & Kim, 1992). However, when tested under limited access conditions neither galanin nor M40 affected fat intake (Corwin, Rowe, & Crawley, 1995). Similar results were obtained with enterostatin, a neuropeptide thought to contribute to fat-mediated satiety (Erlanson-Albertsson & York, 1997). That is, under limited access conditions, enterostatin had no effect on fatty food intake (Corwin & Rice, 1998; Rice & Corwin, 1996, 1998). These findings indicate that the neurobiology of fat intake under limited access conditions is different from the neurobiology of fat intake under other conditions.

Bingeing induced by limited access may resemble substance abuse

Recent studies have been initiated to investigate potential similarities between fat intake induced by limited access and another IEB, substance abuse. Reports from other groups have shown that the GABA-B agonist baclofen reduces drug self-administration in animals (Fattore, Cossu, Martellotta, & Fratta, 2002; Janak & Gill, 2003; Ranaldi & Poeggel, 2002; see also Brebner, Phelan, & Roberts, 2002; Cousins, Roberts, & de Wit, 2002, for reviews), and has shown promise clinically in the treatment of substance abuse and dependence (Addolorato, Caputo, Capristo, Domenicali, Bernard and Janiri, 2002; Assadi, Radgoodarzi, & Ahmadi-Abhari, 2003; Shoptaw, Yang, Rotheram-Fuller, Hsieh, Kintaudi and Charuvastra, 2003; see also Brebner et al., 2002; Cousins et al., 2002, for reviews). Recent data from this laboratory indicate that baclofen reduces binge-type consumption of fat induced by limited access without reducing consumption of a high-fat diet or chow (Buda-Levin, Wojnicki, & Corwin, 2005). This is interesting because bingeing and substance abuse share clinical comorbidity (Brewerton et al., 1995; Bulik et al., 2002; Bushnell et al., 1994; Herzog et al., 1992; Johnson et al., 1997; Laessle et al., 1989; Wiederman & Pryor, 1996; Wilson, 1993) and baclofen generally has no effect on or increases food intake in non-binge animal protocols (Brebner et al., 2000; Ebenezer, 1995; Echo, Lamonte, Ackerman, & Bodnar, 2002; Higgs & Barber, 2004; Minano, Meneres Sancho, Sancibrian, Salinas, & Myers, 1992; Stratford & Kelley, 1997; Ward, Somerville, & Clifton, 2000; Wirtshafter, Stratford, & Pitzer, 1993; Znamensky, Echo, Lamonte, Christian, Ragnauth and Bodnar, 2001). Taken together, these findings suggest that the neural signaling involved in binge-type eating, as modeled in the limited access protocol, is different from that of non-binge eating. Instead, neural signals relevant to the IEB of bingeing may be more closely aligned with those involved in the IEB of substance abuse.

Conclusions

The neurobiology of repeated, intermittent, episodes of behavioral excess is not well understood. However, converging evidence suggests that common mechanisms may contribute to disorders involving this type of behavior. Research from this laboratory has shown that

limited access to shortening can induce repeated, intermittent, excessive consumption of shortening in non-food-deprived rats. The protocol is relatively simple and inexpensive, and the behavior is similar in some ways to human bingeing. Recent data suggest that neural signaling under limited access binge-type conditions is different from non-binge conditions, and may be more closely aligned with substance abuse. There currently are a variety of feeding protocols that can be used to advance our understanding of physiological and neurological alterations that occur as a result of engaging in IEB. Such research is critical if we are to elucidate mechanisms that contribute to development, maintenance, and relapse in these often destructive patterns of behavior.

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