Neuroscience and Biobehavioral Reviews 37 (2013) 1919–1931

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

Mapping brain circuits of reward and motivation: In the footsteps of Ann Kelley

Jocelyn M. Richard*, Daniel C. Castro, Alexandra G. DiFeliceantonio, Mike J.F. Robinson, Kent C. Berridge

Department of Psychology, University of Michigan, 530 Church Street, Ann Arbor, MI 48109-1043, USA

ARTICLE INFO

Article history:
Received 31 August 2012
Received in revised form
27 November 2012
Accepted 10 December 2012

Keywords:
Eating
Pleasure
Fear
Incentive salience
Nucleus accumbens
Neostriatum
Ventral pallidum
Opioid
Dopamine
Rat

ABSTRACT

Ann Kelley was a scientific pioneer in reward neuroscience. Her many notable discoveries included demonstrations of accumbens/striatal circuitry roles in eating behavior and in food reward, explorations of limbic interactions with hypothalamic regulatory circuits, and additional interactions of motivation circuits with learning functions. Ann Kelley's accomplishments inspired other researchers to follow in her footsteps, including our own laboratory group. Here we describe results from several lines of our research that sprang in part from earlier findings by Kelley and colleagues. We describe hedonic hotspots for generating intense pleasure 'liking', separate identities of 'wanting' versus 'liking' systems, a novel role for dorsal neostriatum in generating motivation to eat, a limbic keyboard mechanism in nucleus accumbens for generating intense desire versus intense dread, and dynamic limbic transformations of learned memories into motivation. We describe how origins for each of these themes can be traced to fundamental contributions by Ann Kelley.

Contents

* Corresponding author at: Department of Psychology, University of Michigan, 530 Church Street, 3242 East Hall, Ann Arbor, MI 48109-1043, USA. Tel.: +1 734 764 8078; fax: +1 734 763 7480.
E-mail addresses: jocelyri@umich.edu (J.M. Richard), castrod@umich.edu (D.C. Castro), agdife@umich.edu (A.G. DiFeliceantonio), mikejfr@umich.edu (M.J.F. Robinson), berridge@umich.edu (K.C. Berridge).

0149-7634/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.neubiorev.2012.12.008

1. Introduction

Our thesis here is that discrete psychological components of motivation and reward affect are to some degree assignable to discrete neurochemical and neuroanatomical mechanisms within brain mesocorticolimbic circuitry. Neural manipulations especially can dissociate and reveal these components, sometimes in surprising ways. For example, some particular psychological components that seem closely interconnected in common experience, such as 'wanting' and 'liking' for the same reward, may actually be less similar in neural mechanisms than other motivational components that seem psychologically opposite, such as fear and desire. We describe such components here, and highlight how neuroscience studies of motivation and reward can benefit from combining careful behavioral analyses with neural manipulations and mapping of brain mechanisms. Work by the late Ann Kelley and colleagues began many of these efforts, and inspired related studies in our and others' laboratories aimed at identifying the psychological nature of motivation components and the specific neural systems involved.

2. Nucleus accumbens in eating and 'liking'

Ann Kelley was a leading pioneer in the neuroscience of reward and motivation. For example, she and her colleagues were among the first to combine research on the anatomy of mesocorticostriatal systems, the role of opioid signals in striatal systems, and their interactions with hypothalamic regulatory circuits in controlling motivated behavior. Those investigations by her laboratory followed her earlier collaborative studies with Iversen and colleagues on classic mesolimbic microinjection effects, and her elegant collaborative neuroanatomical studies with Nauta and colleagues in the late 1970s and early 1980s (Kelley et al., 1980, 1982; Kelley and Iversen, 1978).

One important later theme for the Kelley lab concerned reward circuitry underlying generation of the motivation to eat. By the early 1990s, Bakshi and Kelley (1993b) had shown that microinjections of morphine into either nucleus accumbens (NAc; ventral striatum) or ventromedial regions of neostriatum (dorsal striatum or caudate–putamen) caused robust increases in eating behavior and food intake. Following this discovery, Kelley and colleagues went on to demonstrate that eating induced by mu opioid stimulation of NAc was sensitive to the palatability of the food eaten, preferentially enhancing intake of palatable sweet or high fat foods more than other foods, rather than merely instigating a general drive to ingest or engage in oromotor consummatory acts (Kelley et al., 1996; Zhang et al., 1998; Zhang and Kelley, 1997). Those results from the Kelley lab helped develop the idea that mu opioid signaling in NAc might enhance the hedonic impact of palatable foods to stimulate ingestion (Baldo and Kelley, 2007).

Another important issue for Ann Kelley's work was anatomical heterogeneity and localization of function within subregions of striatal structures. To determine which opioid circuits worked to enhance palatable eating, Zhang and Kelley (2000) conducted an extensive opioid microinjection mapping study of behavioral effects on stimulated eating, comparing regions of NAc and neostriatum. They found that opioid stimulation of eating was supported by the entire NAc shell (both medial shell and lateral shell) and entire NAc core, plus ventrolateral regions of neostriatum. In addition, they showed that mu opioid receptor stimulation in the NAc increased Fos expression in other limbic brain structures, such as lateral hypothalamus and ventral tegmental area, indicating recruitment of distributed brain networks to motivate feeding.

3. Pinpointing opioid hedonic enhancement in NAc: discovery of a 'liking' hotspot

Such findings by Ann Kelley and colleagues, together with related work by others (Gosnell and Majchrzak, 1989; Islam and Bodnar, 1990; Simone et al., 1985), inspired many labs to further investigate the role of opioid circuitry in the NAc in palatability. In particular, our lab set out to identify whether and where opioid stimulation would enhance basic positive hedonic reactions of 'liking' to palatable tastes, such as sucrose. Initial taste reactivity experiments found that systemic injections of morphine increased hedonic reactions to sucrose solutions (Doyle et al., 1993; Rideout and Parker, 1996) and decreased aversive behaviors to bitter quinine (Doyle et al., 1993; Parker et al., 1992; Rideout and Parker, 1996). The taste reactivity test of orofacial reactions was developed for rodents receiving intra-oral infusions of taste solutions (Grill and Norgren, 1978; Pfaffmann et al., 1977), and was based originally on earlier demonstrations by Steiner (1973) of distinct positive versus negative affective facial expressions in newborn human infants elicited by sweet (e.g., rhythmic lip-licking) versus bitter or sour tastes (e.g., gapes, headshakes). The microstructure of affective orofacial reactions of 'liking' versus 'disliking' is systematically homologous between rodents, monkeys, apes, and human infants, making taste reactivity a useful tool to empirically study hedonic experiences (Berridge, 2000, 2003; Steiner, 1973; Steiner et al., 2001).

Pecina and Berridge (1995, 2000) approached the localization question for opioid pleasure mechanisms by examining the effects of morphine microinjections on hedonic reactions to sucrose as assessed by the taste reactivity test. First, Pecina and Berridge (1995) found that intracerebroventricular microinjections of morphine into the forebrain lateral ventricles increased hedonic 'liking' reactions to a sweet sucrose taste, confirming that opioids promote eating by acting on central brain mechanisms to enhance the sensory pleasure of food. To more directly investigate the localization of substrates for hedonic enhancement, Pecina and Berridge (2000) subsequently made microinjections of morphine directly into brain sites within the medial shell of NAc, one of the areas where Kelley's studies had found mu opioid receptor stimulation to most potently increase eating (Zhang et al., 1998; Zhang and Kelley, 1997, 2000). Peciña and Berridge found that opioid stimulation of the NAc medial shell was sufficient to enhance hedonic 'liking' reactions to sucrose. But not all sites of medial shell were equally effective: a localized hotspot seemed to exist that doubled or tripled 'liking' reactions, whereas morphine microinjections at other shell sites did not, even though those sites just as powerfully stimulated eating. This grouping of sites turned out to be clumped in the anterior half of medial shell, as viewed by today's understanding of NAc anatomy.

4. Changing criteria for rostrocaudal boundaries in NAc shell

Peciña and Berridge initially adopted the same stereotaxic coordinates as Kelley and colleagues to target the medial shell (Basso and Kelley, 1999; Kelley and Swanson, 1997; Maldonado-Irizarry et al., 1995; Zhang and Kelley, 2000). Most of their sites were located in what we would now classify as the rostral half of medial shell, even sites intended to be relatively caudal. Indeed, most microinjection studies from many labs through the 1990s focused primarily on the rostral half of NAc (for example: Burgdorf et al., 2001; Carlezon and Wise, 1996; Duvauchelle et al., 1992; Hyytia and Koob, 1995; Sills and Vaccarino, 1996; Sokolowski and Salamone, 1998). The caudal half was left relatively unexplored until after 2000.

Caudal neglect of NAc until the 21st century may have arisen in part because popular stereotaxic atlas representations of the caudal