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Neuropeptides and central control of sexual behaviour from the past to the present: A review

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ABSTRACT

Of the numerous neuropeptides identified in the central nervous system, only a few are involved in the control of sexual behaviour. Among these, the most studied are oxytocin, adrenocorticotropin, α-melanocyte stimulating hormone and opioid peptides. While opioid peptides inhibit sexual performance, the others facilitate sexual behaviour in most of the species studied so far (rats, mice, monkeys and humans). However, evidence for a sexual role of gonadotropin-releasing hormone, corticotropin releasing factor, neuropeptide Y, galanin and galanin-like peptide, cholecystokinin, substance P, vasoactive intestinal peptide, vasopressin, angiotensin II, hypocretins/orexins and VGF-derived peptides are also available. Corticotropin releasing factor, neuropeptide Y, cholecystokinin, vasopressin and angiotensin II inhibit, while substance P, vasoactive intestinal peptide, hypocretins/orexins and some VGF-derived peptide facilitate sexual behaviour. Neuropeptides influence sexual behaviour by acting mainly in the hypothalamic nuclei (i.e., lateral hypothalamus, paraventricular nucleus, ventromedial nucleus, arcuate nucleus), in the medial preoptic area and in the spinal cord. However, it is often unclear whether neuropeptides influence the anticipatory phase (sexual arousal and/or motivation) or the consummatory phase (performance) of sexual behaviour, except in a few cases (e.g., opioid peptides and oxytocin). Unfortunately, scarce information has been added in the last 15 years on the neural mechanisms by which neuropeptides influence sexual behaviour, most studied neuropeptides apart. This may be due to a decreased interest of researchers on neuropeptides and sexual behaviour or on sexual behaviour in general. Such a decrease may be related to the discovery of orally effective, locally acting type V phosphodiesterase inhibitors for the therapy of erectile dysfunction.

Contents

Abbreviations: ACTH, adrenocorticotropin; CRF, corticotropin releasing factor; MSH, melanocyte stimulating hormone; GABA, gamma-amminobutirric acid; GALP, galanin-like peptide; GH, growth hormone; GnRH/LHRH, gonadotropin re leasing hormone; LH, luteinizing hormone; NO, nitric oxide; PVN, paraventricular nucleus of the hypothalamus; SO, supraoptic nucleus; VIP, vasoactive intestinal peptide.

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1. Introduction

Sexual behaviour plays a main role in reproduction of all living animals, from insects to mammals, including humans. In mammals, it is commonly accepted that it is organized in two main phases, anticipatory and consummatory, and several quantifiable parameters have been identified in each phase and in both males and females. These studies were conducted mainly in rats because of their availability, the well characterized sequence of copulatory behaviour and its parameters in the male (for a detailed description of the male rat copulatory behaviour see Bitran and Hull, 1987; Sachs, 1978; Sachs and Meisel, 1988, 1994; Hull et al., 2002), and of proceptive and receptive (lordotic) behaviour in the female (see Caggiula et al., 1976, 1979), although data on some other animal species are also available (Absil et al., 1994). Penile erection, seminal emission and ejaculation characterize the consummatory phase of the male sexual response, while vaginal lubrication, clitoris erection and orgasm are typical of the female sexual response. These consummatory responses are preceded by an anticipatory, mainly appetitive phase, which includes motivation towards and searching of an adequate partner for copulation (see Sachs and Meisel, 1988; Meisel and Sachs, 1994). Also in humans the sexual response is organized in distinct and sequential phases, which include usually (but not always) sexual desire followed by sexual arousal and orgasm, including ejaculation in males, when a partner is available for sexual intercourse, although an integration of these phases is likely to exist (see Masters and Johnson, 1966; Kaplan, 1979; Leiblum, 1998). Briefly, when sexual (visual, auditory, olfactory, tactile and in humans even imaginative) stimuli reach the central nervous system, neural pathways are activated which convey sexual information from the higher brain centres through the spinal cord and the autonomous nervous system to the genital apparatus to induce penile erection in males and vaginal lubrication/clitoris erection in female in order to make sexual intercourse, which will culminate with orgasm, feasible (see Meisel and Sachs, 1994; Lue and Tanagho, 1987; Burnett et al., 1992; Raifer et al., 1992; Andersson and Wagner, 1995; Argiolas and Melis, 1995; Argiolas, 2005 and references therein) (Fig. 1). It is well known that numerous neurotransmitters and neuropeptides are involved at central and peripheral level in the control of the above phases of sexual behaviour. Among neuropeptides, oxytocin, adrenocorticotropin (ACTH), α-melanocyte stimulating hormone (α-MSH) and opioid peptides are the most studied (see Bertolini and Gessa, 1981; Pfaus and Gorzalka, 1987; Dornan and Malsbury, 1989; Argiolas, 1999). These neuropeptides exert their effect on sexual behaviour by acting mainly in the hypothalamus and its nuclei (e.g., lateral hypothalamus, paraventricular nucleus, ventromedial nucleus, arcuate nucleus), the medial preoptic area and in other brain areas as well (e.g., the ventral tegmental area, the hippocampus, the amygdala, the medulla oblongata and the spinal cord), where they often interact in a concerted manner with classical neurotransmitters, such as dopamine, glutamic acid, gamma-amminobutirric acid (GABA), nitric oxide and others to influence either sexual performance or sexual motivation and arousal or both (see Argiolas and Melis, 2004, 2005; Melis and Argiolas, 2011; Andersson, 2011; Baskerville and Douglas, 2008; Baskerville et al., 2009). However, evidence also exists for a role of gonadotropin-releasing hormone (GnRH or LHRH), corticotropin releasing factor (CRF), vasoactive intestinal peptide, neuropeptide Y, galanin, galanin-related peptide, cholecystokinin, substance P and neurokinins, vasopressin, angiotensins and hypocretins/orexins (see Argiolas, 1999; Dornan and Malsbury, 1989). A possible role for a few other peptides, such as VGF-derived peptides and endogenous growth hormone (GH) peptide secretagogues in the control of specific aspects of sexual behaviour, mainly penile erection, also has been suggested (see Argiolas and Melis, 2005) (Tables 1 and 2).

The aim of this work is to review the literature on the central role of the above and newly discovered neuropeptides on sexual behaviour analysed possibly in its main phases, anticipatory and consummatory (see Bitran and Hull, 1987; Meisel and Sachs, 1994; Melis and Argiolas, 1995a; Hull et al., 2002), in the male and female animals of the species more studied so far (e.g. rats, mice, monkeys) and when available, also in humans and in other mammals. Since the literature on the sexual role of some of the above neuropeptides at the central level has been extensively reviewed up to 1999 (Bertolini and Gessa, 1981; Pfaus and Gorzalka, 1987; Dornan and Malsbury, 1989; Richard et al., 1991; Argiolas and Gessa, 1992; Carter, 1992; Meisel and Sachs, 1994; Argiolas, 1999), particular attention was given to the studies appeared since 2000 up to today on the role of oxytocin, ACTH–MSH peptides, opioid peptides and GnRH, because

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