

Oxytocin: An Important Aspect for Designing Neuropsychiatric Drugs

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Abstract

The hormone oxytocin (OT) has a central action where it acts as a neuromodulatory peptide and exerts its action depending upon the distribution of OT receptors (OTR) in the target site. OTRs are G-protein-coupled receptors (GPCRs) comprising different subunits (Gq, Gi, and Gs) and have the ability to activate different pathways, but specific agonists and antagonists may show different affinities to OTRs, depending on the specific G-protein isoform to which they are coupled. In recent study it has been found that OTR distribution varies with age and species and in regions of the brain, region-specific expression of different receptors could be important in the development of new drugs targeting specific neuropsychiatric disorders.

Keywords: Neuropeptide; Neurotransmitter; Receptor; Neuromodulation

Introduction

OT (oxytocin) is a neuropeptide synthesized in the hypothalamus by paraventricular (PVN) and supraoptic nuclei (SON), and secreted by the posterior pituitary lobe into blood circulation [1,2]. In central action OT is a neurotransmitter but, in peripheral action, OT is a hormone and is involved in different physiological and pathological functions like sexual activity, penile erection, ejaculation, pregnancy, uterus contraction, milk ejection, maternal behavior, social bonding etc. [3].

Brain neuropeptide OT has been shown to affect social processes in animals; this molecule and its receptors participants in the treatment of neurodevelopmental disorders [4]. Classical neurotransmitters are packaged in small synaptic vesicles and are localized at vesicles [3].

However, peptides are stored in large dense-core vesicles (LDCV) which are distributed in soma, dendrites, axonal, as well as nerve endings of magnocellular neurons of the paraventricular nucleus in different regions of the brain [5]. Oxytocin from the hypothalamus reaches different regions of the brain by axonal release from the OT containing fibers that specifically target areas of the brain expressing its receptors [6].

Oxytocin receptors (OTR) are members of the G-protein coupling receptor (GPCR) superfamily. The gene of the OTR contains 3 introns and 4 exons and is located in a single copy on chromosome 3p25, and the structure of GPCRs is characterized by seven transmembrane (7-TM) α -helices connected by three intracellular (IL-1 to IL-3) and three extracellular loops (EL-1 to EL-3) [1]. These receptors can be coupled to different G-proteins, and

exhibit different functions. Oxytocin receptor coupled with heterotrimeric Gq/11 protein activates the phospholipase C β pathway (PLC β), causing the release of Ca²⁺ from intracellular stores and increases neuronal excitation [7], thereby enhancing GABA release from interneurons [8,9]. Besides this, Gq/11 family of proteins consists of four members, two of which (Gq and G11) are almost expressed in the central nervous system [10]. This is responsible for maternal behavior after parturition in females [11].

Apart from this, oxytocin can also activate inward rectifying current through Gi/o protein, which is also responsible for the antiproliferative effect [12]. In addition to this, the protein Gs of oxytocin receptor can also increase cAMP production by activating adenylate cyclase, which opens sodium channels inwards [3].

Central Action of Oxytocin

Social bonding is important factor for survival of organism because it favours reproduction, protection against predator, environmental changes, and brain development [13]. There are wide range of well known neurotransmitters (dopamine, endorphins) involved in the process of synaptic activity formation and regulation of social behavior [14]. In response to external environmental interaction and stimuli, neural circuit are plastic [15], such plasticity is enabled by the release various neuromodulators [16-20].

Neuromodulation is a process of sensory processing, which affect attention or increase the salience of incoming inputs to aid encoding of behaviorally-important experiences [15]. In central nervous system OT is a one neuromodulator of social behaviors, OT and its receptor hold a leading position in the substance of happiness, and function as a important compound of brain building trust, emotional relationship, therefore also known as love hormone [14,21]. Central release of oxytocin express important behaviors such as pair bonding and maternal care of infants [18,22]. A recent study demonstrated that long term administration of OT increase trust and enhance attachment among organism, such finding could help treatment of social disorders like phobia and autism [14,23].

Apart from this stress and anxiety can alter motherhood and lactation, therefore OT control stress and anxiety during lactation which may be mediated by an influence of OT on dopaminergic neurotransmission in limbic brain regions [24]. It is well documented in

previous study women with panic disorder can feel relief during lactation period [25].

Therefore, interest is growing towards the study of neuropeptides and their region-specific receptors that may be important when designing new drugs targeting specific neuropsychiatric diseases [26,27].

From the above study we can conclude that G protein isoforms have the ability to activate different pathways, but specific agonists and antagonists may show different affinities to OTRs because, their action depends on the specific G protein (Gq, Gi or Gs) to which they are coupled and region-specific expression of different receptors could be important for the development of new drugs targeting specific neuropsychiatric disorders.

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