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Neuroanatomy of Affective Touch Sensation

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ABSTRACT

The neural substrates involved in the tactile experience of soft or gentle touch have long been elusive but are now identified with some certainty. The neuropeptide prokineticin 2 appears to be involved in the encoding and transmission of pleasant touch to specific regions of the brain. This somatosensory pathway, refined in human primates, seems to be crucial in human social development and behavior. These findings may have important implications in the prevention and treatment of some common mental disorders as well as building resilience in coping with the stresses of modern life experience.

Keywords: Prokineticin 2; Pleasant Touch; Neurobiology; Neuropsychiatry

Introduction

Touch is central to interpersonal interactions and is one of the four main modalities of somatic sensation. Each relay either touch, heat, pain or pruritic (itch) information to the central nervous system. Apart from localized discrimination in space and time, touch also provides the subjective experience of affiliative or emotional somatic pleasure (McGlone, et al. [1]). Affective processing in skin-brain pathways has wider implications for the exchange of social information (Morrison, et al. [2]) and behavioral development (Bales, et al. [3]). Affective or pleasant touch such as stroking, caressing or hugging is an essential part of human behaviour. Complex molecules acting as neurotransmitters are involved including some that act as hormones such as oxytocin. The latter is well known for its role in generating feelings of attachment and affection (Shen, 2015) Interpersonal affective touch has an important role in mental health and plays a crucial part in social interactions including human development (Cascio, et al. [4]). Pleasant touch seems to provide emotional and psychological support that helps mitigate social isolation and stress (Chen [5]). However, the way in which pleasant touch information is encoded and transmitted from sensory neurons to the spinal cord - and the brain, remains somewhat uncertain.

Spinal Circuitry

Liu and colleagues (Bao, et al. [6]) identified interneurons in the spinal cord dorsal horn that express prokineticin receptor 2, as well as sensory neurons that express a binding molecule, or ligand, the neuropeptide prokineticin 2. These are involved in the encoding and transmission of pleasant touch. Chen showed that genetic ablation of these neurons in mice selectively abolished the pleasant touch-conditioned place preference test whilst preserving other sensations. These mutant mice display profound impairment in stress response and prosocial behaviour (Chen, et al. [7]). The subjective experience of emotional pleasure of touch seems to be mediated by a class of slow, unmyelinated peripheral nerve fibres with specific neurobiological and electrophysiological properties (McGlone, et al. [1]) that synapse in the spinal cord to produce this ligand or neuropeptide.

Mammalian and Primate Brain Pathways

Hang Yu and colleagues showed that social touch- like stimulation enhanced the firing of oxytocin neurons in the mouse paraventricular hypothalamus (Yu, et al. [8]). This pleasant sensory experience promoted social interactions and social behaviour with

positive reinforcement of place preference. In primates, presumably including humans, social grooming (affective touching) clearly plays a particularly important role in social bonding. This has a major impact on social development and an individual's lifetime reproductive fitness. There is strong evidence from comparative brain analysis that primates have social relationships of a qualitatively different kind to those found in other animal species (Panksepp [9] and Hertenstein, et al. [10]) with social grooming acquiring a new function. Dunbar has reviewed the evidence for a neuropeptide basis for social bonding (Dunbar [11]) with the neuroendocrine pathways involved demonstrating the central importance of oxytocin and endorphins. These two neuropeptides may play different roles however in the processes of social bonding in both primates and non-primates. The rewarding properties of social interaction in mice require the coordinating activity of oxytocin and the serotonin receptor 5HT in the nucleus accumbens (Dolen, et al. [12]). This has implications for understanding the pathogenesis of social dysfunction in neuropsychiatric disorders such as autism, discussed below.

Human Studies

Functional magnetic resonance imaging (fMRI) studies have been used to elucidate the unique different cortical signals in response to passive touch, both active and slow (Ackerley, et al. [13,14]) examined the relationship between the neural response and individuals' social abilities in 19 healthy adults. Connectivity analysis revealed co-activation of the medial prefrontal cortex, orbitofrontal cortex, amygdala and insular cortex during slow touch. However, in participants with autistic traits, there was negative correlation to slow touch in some of these regions. The Voos study supports previous findings of the involvement of a network of "social brain regions" that process slow, unmyelinated afferent peripheral nerve fibres mediating affective touch (C tactile or CT system) as well as highlighting the multimodal nature of this system. The variability in the brain response to affective touch also illustrates a tight coupling of social behaviour and social brain function in a cohort of typical adults. In (Kirsch, et al. [15]) and colleagues reported studies addressing neurophysiological specificity in the communication of emotions by touch.

Blindfolded participants were touched without any contextual cues, and asked to identify the touch provider's emotion and intention. Affiliative emotions such as love, or social support were reliably elicited by gentle, soft touch whether delivered by CT optimal velocities (3cm/s) or CT suboptimal velocities (18cm/s). However the CT optimal velocity gentle touch participants were significantly more likely to report arousal, lust or desire. This suggests that other "top-down" factors contribute to these aspects of tactile social communication. The posterior insular cortex is considered the primary cortical target of CT afferents and temporal cortex involvement has been linked to more affiliative aspects of CT optimal touch. This paradigm was tested by Kirsch in a stroke patient with right perisylvian damage including the insular cortex but excluding temporal cortex on MRI studies. He showed impairment in "reading" emotions based on CT optimal (3cm/s) touch. This study by Kirsch and colleagues suggest that the CT system can add specificity to emotional and social communication, particularly with regards to feelings of desire and arousal. On the basis of these findings they speculate that its primary functional role may be to enhance the "sensual salience" of tactile interactions in humans.

Touch and Human Development

Interpersonal touch influences neural and behavioral development throughout life (Bales, et al. [3]). Mental retardation in infants emanating from the notorious charity orphanages of Romania in the Soviet era (Nelson, et al. [16]) demonstrates the powerful force of touch in human development. The children in the orphanage were deprived of human touch and it is clear that disruption in early social-sensory input during infancy has severe developmental consequences throughout the life span. Social touch is important for cognition, attachment, communication and emotional regulation from infancy (Cascio, et al. [4]). The quality of touch matters with gentle stroking touch generating increased smiling, a lowered heart rate and increased engagement in infants. The pattern of neural responses to CT targeted touch appears similar in school age children as in adults, namely the posterior insular and posterior superior temporal sulcal regions. This circuitry for social touch continues to mature as the brain develops (Bjornsdotter, et al. [17]).

Cascio and colleagues reviewed the role of social touch in disordered development using as an example the autism spectrum disorder. Avoidance of social touch in infancy is a predictor of autism spectrum in older children (Mammen, et al. [18]). It seems clear that social touch plays a critical role in the neural, behavioural and physiological growth and advancement of infants and young children through to adolescence and adulthood. Far reaching epigenetically mediated effects on development have been broadly studied in the context of critical windows in the social and physical environments in humans (Szyf [19]). Parental touch is linked to oxytocin levels in parents (Feldman, et al. [20]) and this has effects on later social-emotional behavioural issues in children that are associated with maternal anxiety (Pickles, et al. [21]).

Social Touch in the Covid-19 Pandemic

Social distancing regulations and lockdowns during the pandemic reduced the ability to engage in personal touch. Meijer and colleagues conducted an online survey of nearly 2000 people in regard to the effect of these regulations. Participants reported

feelings of longing for touch which increased with the duration and severity of the COVID-19 restrictions. There was also an associated increase in the perceived pleasantness of observing touch. Stress also seems to respond in a positive fashion to social touch and assists with adaptation to adversity (Dagnino Subiabre [22]) as witnessed in the COVID-19 pandemic. Whilst there are several factors affecting stress resilience, social behaviour inclusive of social touch seems vital. It may be possible in the future to modulate stress resilience through the stimulation of low threshold CT-fiber mechanoreceptors. This technology may have a role in the prevention of stress related neuropsychiatric disorders including social avoidance, acute anxiety and major depression [23-29].

Conclusion

The ligand prokineticin 2 has now been identified as the neuropeptide that encodes and transmits social or pleasant touch to the equivalent, appropriate spinal neurons. These findings have important implications for elucidating mechanisms by which pleasant touch deprivation contributes to brain development and mental disorders. Social touch in infancy has far reaching sequelae throughout the developing brain and it continues to influence brain development beyond infancy. Furthermore, it appears that this somatosensory system plays a key role in translating the socio-emotional information of social touch into active coping with stress and building stress resilience in the longer term.

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