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Socio-sexual processing in cortical circuits

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How does social and sexual information processing map onto cortical circuits? Addressing this question has been difficult, because of a lack of circuit-oriented social neuroscience and an absence of measurements from interacting brains. Recent work showed social information is already differentially processed in the primary sensory cortices. Converging evidence suggests that prefrontal areas contribute to social interaction processing and determining social hierarchies. In social interactions, we identify gender in split seconds, but after centuries of anatomy we are still unable to distinguish male and female cortices. Novel data reinforce the idea of a bisexual layout of cortical anatomy. Physiological analysis, however, provided evidence for sex differences in cortical processing. Unlike other cortical circuits, sexual processing circuits undergo major rewiring and expansion during puberty and show lasting damage from childhood abuse.

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Introduction

Having observed a correlation between relative cortical volume and average group size, the anthropologist Robin Dunbar [1] hypothesized that the large primate brains may have evolved to process social (as opposed to ecological) information [2]. The importance of sociality is also underscored by its absence: social isolation and deliberate social exclusion are hurtful and have long lasting deleterious effects on the brain and behavior [3]. How then, has social information processing shaped cortical circuits? We address this question from a socio-sexual perspective. We ask, what is special about the processing of social information, how does it differ across cortical regions and does it differ between the sexes? Answering these questions is not straightforward. Research on cortical circuits has been shaped by the systematic study of stimulus response contingencies. Most of the data comes from head-fixed animals and humans in scanners rather than from interacting subjects. Embracing the inherently uncontrolled nature of social interactions is both a conceptual and experimental challenge for neurobiologists. Nonetheless, recent methodological advances have helped in studying animals performing their natural behaviors. In this review, we focus on the processing of social information by cortical circuits. We begin by highlighting recent progress in cellular and circuit-oriented research on the processing of social signals in the primary sensory cortices. We then feature novel technical advances that have enabled the brain-wide analyses of social interactions. Next, we review three high level circuits involved in the processing of faces, social interactions and social memory. Finally, we dwell on cortical circuits processing sexual information.

Processing of social signals in primary sensory cortices

Early work on primary sensory cortices focused on elementary stimulus features and did not provide much evidence for social information processing. Contrary to naïve assumptions that social stimulus would elicit responses comparable to non-social stimuli, recent evidence suggests that social information is already differentially processed (often by spike rate increases) in early sensory cortices. There is also increasing evidence for multisensory integration in some of the cortices described below.

Primary somatosensory cortex, S1

Social facial touch is differentially processed in the primary somatosensory cortex of rats. Extracellular tetrode recordings in freely interacting rats revealed stronger spike responses during facial touch compared to object touch [4]. This key finding demonstrated the occurrence of socially induced response changes in primary sensory areas. In line with this, membrane potential recordings in head-restrained rats show much stronger locking to rhythmic whisking when a conspecific is touched compared to an object. Further membrane fluctuations occur already prior to social touch [5], suggesting an internal origin of social response enhancement. Similar observations were made in a human imaging study, in which male subjects showed increased responses to female touch, and this arose from their mental assignment of tactile contacts to a male or female agent rather than from differences in actual contact patterns [6]. A unique and strictly social

tactile behavior is ticklishness: an old idiosyncratic form of physicalness shared by rats and humans [7]. The trunk somatosensory cortex contains neural mechanisms that contribute to the expression of ticklishness. Specifically, cells in this area are activated in a mood-dependent manner by tickling. Their firing increased prior to and during ultrasonic calls associated with tickling; and stimulation in layer 5 neurons evoked calls suggesting a cellular link between tickling and laughter [8•].

Primary auditory cortex, A1

Maternity associated changes in the auditory cortex are responsible for pup retrieval behavior. When isolated, pups vocalize specific calls and their mothers (but not virgin females) show retrieval behavior (Figure 1a). Inactivation of the left auditory cortex led to a decrease in pup retrieval suggesting lateralization (Figure 1b). Oxytocin receptor expression was also lateralized (Figure 1c) suggesting its involvement in pup retrieval. Indeed, the application of oxytocin to the left auditory cortex was sufficient to elicit pup retrieval in virgins (Figure 1d) by modulating the cortical excitation/inhibition balance [9••]. These results are important as they not only reiterate the occurrence of social modulation in primary sensory areas but also demonstrate the intersection of these effects with neuroendocrinological/maternal status and the cell type specificity of these effects. Interestingly, changes in feedforward inhibition appear to underlie the maternity-associated increased behavioral responsiveness to pup calls in mice [10]. Multisensory integration of olfactory [11] and tactile [12] has also been reported to alter responses to sound in the auditory cortex.

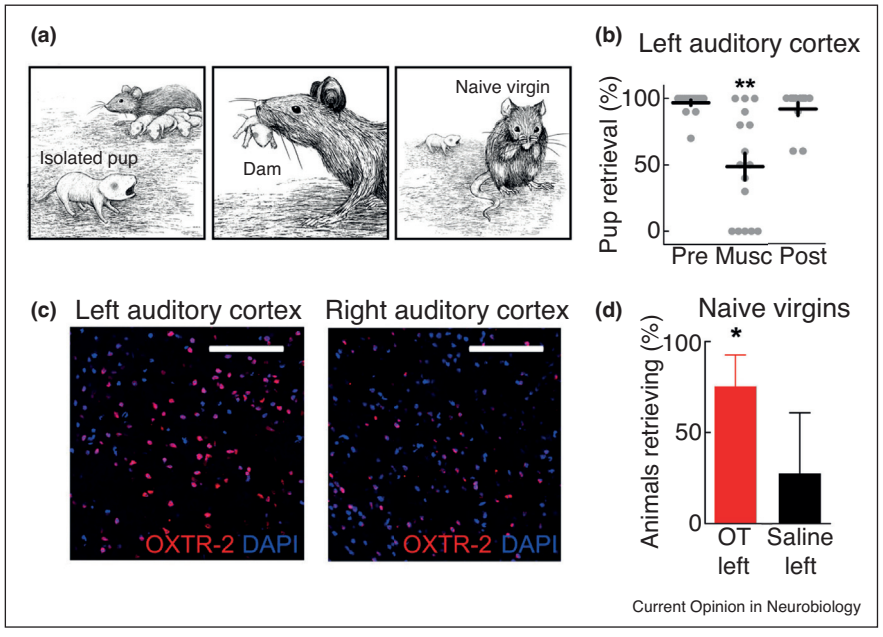
Primary visual cortex, V1

We have a very limited understanding as to how primary visual cortex responds to the sight of a conspecific. This dearth of data is regrettable, as indirect evidence suggests that social stimuli can greatly alter ocular dominance plasticity in visual cortex [13].

Piriform cortex

Olfactory investigation (especially in the form of anogenital sniffng) is a hallmark of rodent social interactions [14]. In addition, extensive exchange of olfactory information occurs during facial interactions, which has been extensively documented in the case of socially transmitted food preference [15]. Similar to the auditory cortex, oxytocin also appears to be involved in modulating the piriform cortex. It has been shown to affect olfactory processing and influence social recognition but not odour processing or recognition in a non-social context [16]. A particularly interesting study (albeit with no piriform responses measured) demonstrated that human subjects increased sniffing of their own hands after shaking hands with others [17].

Figure 1



Oxytocin modulates pup retrieval behavior. **(a)** Isolated pups express ultrasonic calls (left), which lead to pup retrieval behavior expressed by dams (middle) but not by virgin mice (right). **(b)** Musicmol infusion into left auditory cortex decreases dam pup retrieval behavior. **(c)** Oxytocin receptor expression is lateralized to left auditory cortex. **(d)** Virgins injected with oxytocin to their left auditory cortices express pup retrieval. *Source*: Reprinted from Ref. [9••] with permission from Springer Nature.