Fasciola cinereum: once a stranger

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Social familiarity emerges from social novelty through the consolidation of brief encounters into enduring memory representations. In a recent study published in *Vita*, Qin and colleagues trace this process along the projections from hypothalamic supramammillary nucleus (SuM) to a long-overlooked hippocampal subfield — the fasciola cinereum (FC) — and find that novelty signals from the SuM are transformed into a familiarity-related signal in the FC. The newly identified circuit elucidates how social familiarity is constructed, establishing the FC as a computationally distinct hub within the canonical hippocampal social-memory circuit.

In "*The Little Prince*", Saint-Exupéry's fox describes how familiarity can turn one fox among a hundred thousand into one "unique in all the world". What trace does a fleeting encounter leave in the brain, allowing novelty to give way to familiarity? Qin *et al.* now place the fasciola cinereum (FC) at the heart of this question[1]. Nestled at the caudal pole of the hippocampus, wedged between CA1 and the third ventricle, the FC forms a slender bridge of grey matter across the midline whose function has long remained obscure. Anatomically distinct yet functionally enigmatic, this diminutive hippocampal subfield has only recently emerged in studies of seizure propagation and visual contextual memory[2,3]. These disparate findings offered glimpses of its importance without revealing the computation it performs. In this issue, Qin *et al.*[1] uncover a previously unknown circuit that drives new-to-known transition: rapid plasticity driven by repeated social encounters links the fading of hypothalamic novelty signals to the rise of a familiarity-related FC response.

Early gene-expression mapping suggested a molecular continuity between FC and CA2[4], the hippocampal subfield classically associated with social memory. At the circuit level, however, a different picture emerges: although FC also receives dense monosynaptic input from SuM, a hypothalamic source of novelty signals[5], FC-projecting SuM neurons showed negligible overlap with those targeting CA2 or DG. Behavioral perturbations then discovered what the SuM–FC circuit is needed for. Normally, mice are naturally drawn to an unfamiliar conspecific but spend progressively less time investigating the same animal across repeated encounters. Silencing SuM–FC terminals during those initial meetings prevented this decline in interest; yet turning off the same terminals during a later memory test did not prevent mice from distinguishing the familiar animal from a newcomer. Suppressing SuM-recipient FC neurons, by contrast, compromised both the development of familiarity and its later expression. These effects appeared relatively selective for social memory, as comparable manipulations spared object recognition and contextual fear memory. This asymmetry across learning and recall suggests that SuM provides an instructive signal during the encounter with an unfamiliar conspecific, whereas FC remains engaged once novelty has faded and familiarity has taken hold. Intriguingly, broad optogenetic activation of FC recipient neurons did not improve memory and could instead impair recall, suggesting that familiarity depends on the precise pattern of FC activity rather than on a simple increase in overall firing.

The most conceptually striking finding is the functional inversion in the SuM–FC pathway. Single-unit recordings in freely moving mice showed that FC-projecting SuM neurons fired vigorously upon first exposure to a novel conspecific and progressively attenuated with repeated meetings. This relationship flips in FC, where activity increased as the same conspecific became familiar. The pathway thus behaves like a neural NOT gate: "novel" in, "familiar" out. Yet, how the circuit executes this sign reversal remains unresolved.

One possible substrate for this inversion comes from the rapid cellular plasticity that accompanies social familiarization. After repeated encounters, SuM-recipient FC neurons became more excitable, and excitatory SuM–FC synapses underwent potentiation, as reflected in larger evoked EPSCs and higher AMPA/NMDA ratio, while inhibitory transmission remained comparatively unchanged. Thus, these adaptations could help amplify FC output as the upstream novelty signal subsides. The authors next used optogenetic manipulation to weaken or strengthen SuM–FC synapses, establishing a causal role for their plasticity in sustaining social memory. Induced LTD at SuM–FC synapses via low-frequency light stimulation after social familiarity had already been established could erase the established memory: LTD-treated mice renewed their interest in a previously familiar animal, much as they would toward a stranger. Conversely, optogenetically induced LTP at the same synapses helped turn a passing encounter into a remembered acquaintance.

By integrating projection-defined neural recordings, causal circuit perturbations and synaptic physiology, Qin *et al.* establish FC as a familiarity hub driven in the hypothalamus and identify the SuM–FC pathway as a direct interface between social novelty and familiarity. This defined circuit provides a powerful model for dissecting the neural computations underlying social familiarization. Qin *et al.* further embed this

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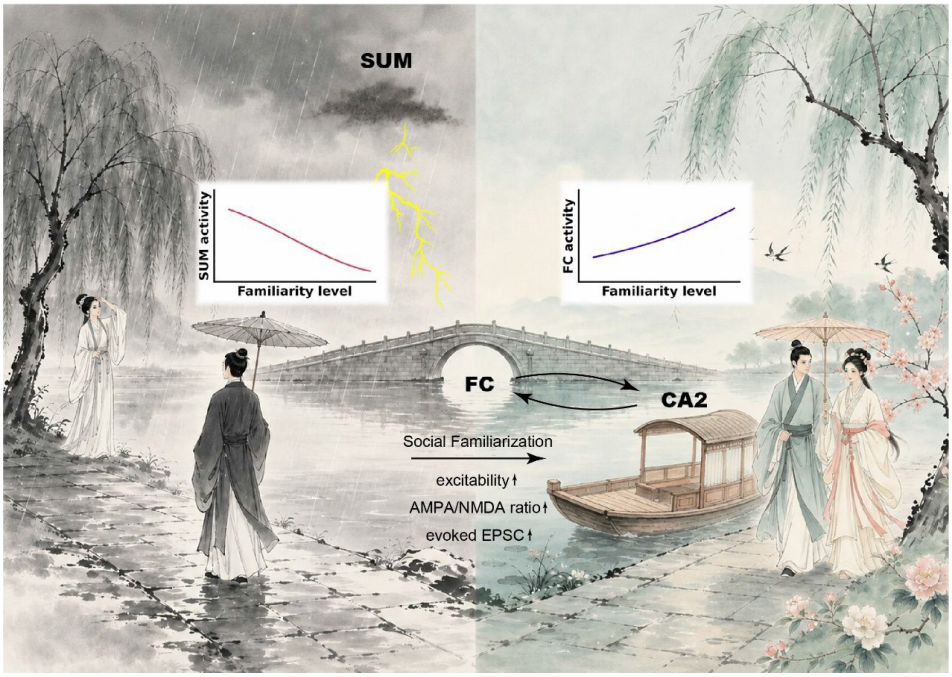

Fig. 1 Bridging stranger and auld acquaintance through the SuM–FC pathway. Novel social encounters strongly activate FC-projecting SuM neurons (the cloud) whose activity wanes across repeated interactions, while downstream SuM-recipient FC neurons (the stone bridge) show the opposite trajectory. Social experience increases FC excitability and potentiates excitatory SuM–FC synapses, leaving a lasting yet flexible imprint that supports the expression of familiarity. Reciprocal connectivity with CA2 may route this familiarity-related FC signal into the broader hippocampal social-memory network. This figure was created with the assistance of generative AI.

process within the canonical hippocampal social-memory network[6,7]: FC reciprocally connected with CA2, and suppressing SuM-recipient FC neurons reduced CA2 activity. In the absence of a direct FC–vCA1 projection, these findings suggest that FC may relay social information through CA2, indicating a working model via FC→CA2→vCA1 flow. Yet FC may not simply recapitulate CA2 function. Its dendritic architecture, afferent organization and network physiology differ markedly from CA2, raising the question of whether the two regions perform complementary computations or successive transformations along the same social-memory stream (Fig. 1).

Remarkable in both scope and mechanistic depth, this work opens a series of inspiring questions about how familiarity is represented, updated and preserved. For example, how does FC preserve an acquaintance while remaining ready for the next stranger? A new conspecific rapidly returns FC firing toward baseline even though prior familiarization has already increased FC excitability and strengthened SuM–FC excitatory synapses. How can a new conspecific reset FC activity while the underlying plasticity persists? What, in turn, does FC activity encode — familiarity itself, or also individual identity and social context[8–10]? Moreover, what circuits govern the striking inversion between falling SuM activity and rising FC output? The cellular adaptations uncovered here indicate that additional mechanisms — including feedforward inhibition, or other FC afferents or reciprocal interactions with CA2 — also should be involved during social familiarization. With these mechanisms coming into focus, the functional roles of FC may help illustrate how time spent together allows the brain to build something as deceptively simple yet biologically profound as social familiarity.

COMPETING INTERESTS

The authors declare no competing interests.

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ADDITIONAL INFORMATION

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