

Cerebellum function: The chronometry of social perception

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<https://doi.org/10.1016/j.cub.2024.03.028>

The posterior cerebellum is emerging as a key structure for social cognition. A new study causally demonstrates its early involvement during emotion perception and functional connectivity with the posterior superior temporal sulcus, a cortical hub of the social brain.

The cerebellum, once confined to the role of mere motor controller, is now emerging as an unsuspected contributor to social life. Our understanding of its functional properties has advanced significantly in recent decades, challenging traditional views¹. Early explorations of the cerebellum's role in emotion began in the '70s², gaining momentum in the late '90s with the identification of Schmahmann's syndrome — also known as cerebellar cognitive affective syndrome — characterized by cognitive and emotional deficits following lesions in the posterior sector of the cerebellum³. These initial observations laid the groundwork for acknowledging the importance of the posterior cerebellum in functions beyond motor control, including those essential for navigating the complexities of social interactions.

Research on the cerebellum's involvement in social cognition is recent, emerging with vigor in the last decade⁴. Despite its youth, this field has yielded significant insights, unequivocally demonstrating the cerebellum's critical role in this domain, ranging from basic processes like emotion recognition to more complex operations involved in mentalizing (see recent reviews and meta-analyses^{5–7}). These functions are underpinned by a more extensive network involved in processing social information, often referred to as the 'social brain'⁸. Among its key components is the posterior superior temporal sulcus (pSTS), a region specialized in analyzing social cues⁹ and closely connected to the cerebellum^{4,10,11}.

However, despite a decade of intense research focusing on the role of the

posterior cerebellum in social cognition, very little is known about the temporal dynamics of its cognitive operations due to the challenge of studying human cerebellar activity with high temporal resolution techniques such as electroencephalography or magnetoencephalography. Another key question mark lies in how the cerebellum interacts with other cortical regions within the social brain to enable accurate social perception. It is important to acknowledge that evidence regarding the cerebellum's connectivity with cortical regions largely relies on animal anatomical studies and correlational imaging studies in humans. This underscores the necessity for complementary approaches to establish, with a causal stance, the nature of cerebellar–cortical interactions and their relevance to human social cognition.

In this issue of *Current Biology*, Ciricugno, Ferrari and colleagues¹² introduce a significant advancement in the study of the posterior cerebellum, focusing on the temporal dynamics of its causal involvement in perceiving emotions from facial expressions, a fundamental aspect of social cognition. The first two experiments employed online interferential transcranial magnetic stimulation (TMS) of the left paravermal cortex, leveraging the temporal precision of the technique to disrupt the cerebellar activity at different timepoints during an emotion discrimination task (Figure 1A). Participants were asked to recognize whether two consecutive emotional faces displayed the same or different emotions; interferential online TMS was

applied at different narrow timepoints after the onset of the second face, on different cortical sites (early visual areas V1/V2, the cerebellum, the pSTS and the vertex). By measuring the impact of TMS on task accuracy, the study revealed the cerebellum's causal influence on emotion perception within a critical window of ~100–200 milliseconds following the presentation of emotional faces, marking the study's first novel contribution to the field. Of note, the results suggested a parallel operation of the cerebellum and pSTS, evidenced by similar disruptions in task performance when interfering with either region within the same temporal window. Moreover, a control condition ruled out the possibility that the observed effects could be ascribed to the spreading of the magnetic field to nearby early visual areas (V1/V2), whose direct stimulation disrupted performance at an earlier timing compared to the cerebellum and pSTS.

These first results prompted the authors to propose that the posterior cerebellum and pSTS might work in tandem and nearly simultaneously. However, other scholars¹³ have proposed a hierarchical processing model for visual information between the cerebellum and pSTS. Building upon evidence from diffusion tensor imaging (DTI)¹¹, functional magnetic resonance imaging (fMRI)^{7,13}, and anatomical cerebellar–cortical pathways in primates¹, it has been suggested that visual information is first relayed from extrastriate visual areas to the pSTS⁹, then to the cerebellum¹³ and from there, in a feedback loop, back to the pSTS.

In their last experiment, Ciricugno, Ferrari *et al.*¹² further advanced our

understanding of this circuit by adopting a condition-and-perturb TMS approach^{14,15} to provide causal evidence in support of feedback connections from the cerebellum to pSTS (Figure 1B). The authors conditioned the left paravermal cortex, transiently altering its functionality through low-frequency repetitive TMS (1 Hz rTMS). Then, they demonstrated that such conditioning nullified the perturbation effect caused by online TMS over the right pSTS, whereas targeting a control area did not. Therefore, by applying multiple TMS paradigms, the authors demonstrated that the effect of pSTS stimulation depended on cerebellar activity, providing causal evidence that cerebellar-to-pSTS functional projections are indeed relevant to emotion recognition. These exciting findings add to the growing body of evidence that highlights the critical role of the posterior cerebellum in social cognition, thereby further emphasizing its relevance beyond motor functions.

These findings warrant consideration within the context of studies investigating brain stimulation, cerebellar connectivity, and the social brain. Prior work has reported changes in motor excitability¹⁶ and glucose metabolism over an extended network of brain regions¹⁷ following low-frequency rTMS of the cerebellum. The affected network encompasses sensorimotor areas such as the premotor and parietal cortices, as well as medial prefrontal areas and portions of the superior and middle temporal gyri¹⁷, proximal to the pSTS site targeted in Ciricugno, Ferrari *et al.*'s study¹². Remarkably, all these cortical regions largely overlap with the social brain, and cerebellar low-frequency rTMS may have thus exerted a widespread effect on this network. Such an effect could potentially contribute to the state-dependency observed in the impact of pSTS stimulation in Ciricugno, Ferrari *et al.*'s study. Moreover, the effect implies that other nodes of the social brain could similarly depend on cerebellar modulation. This raises an important avenue for future research on cerebellum connectivity, involving tasks that assess distinct aspects of social cognition mediated by distinct branches of the social brain.

The pSTS traditionally sits at the heart of this network^{8,18}. It acts as a hub, receiving input from lower-order visual

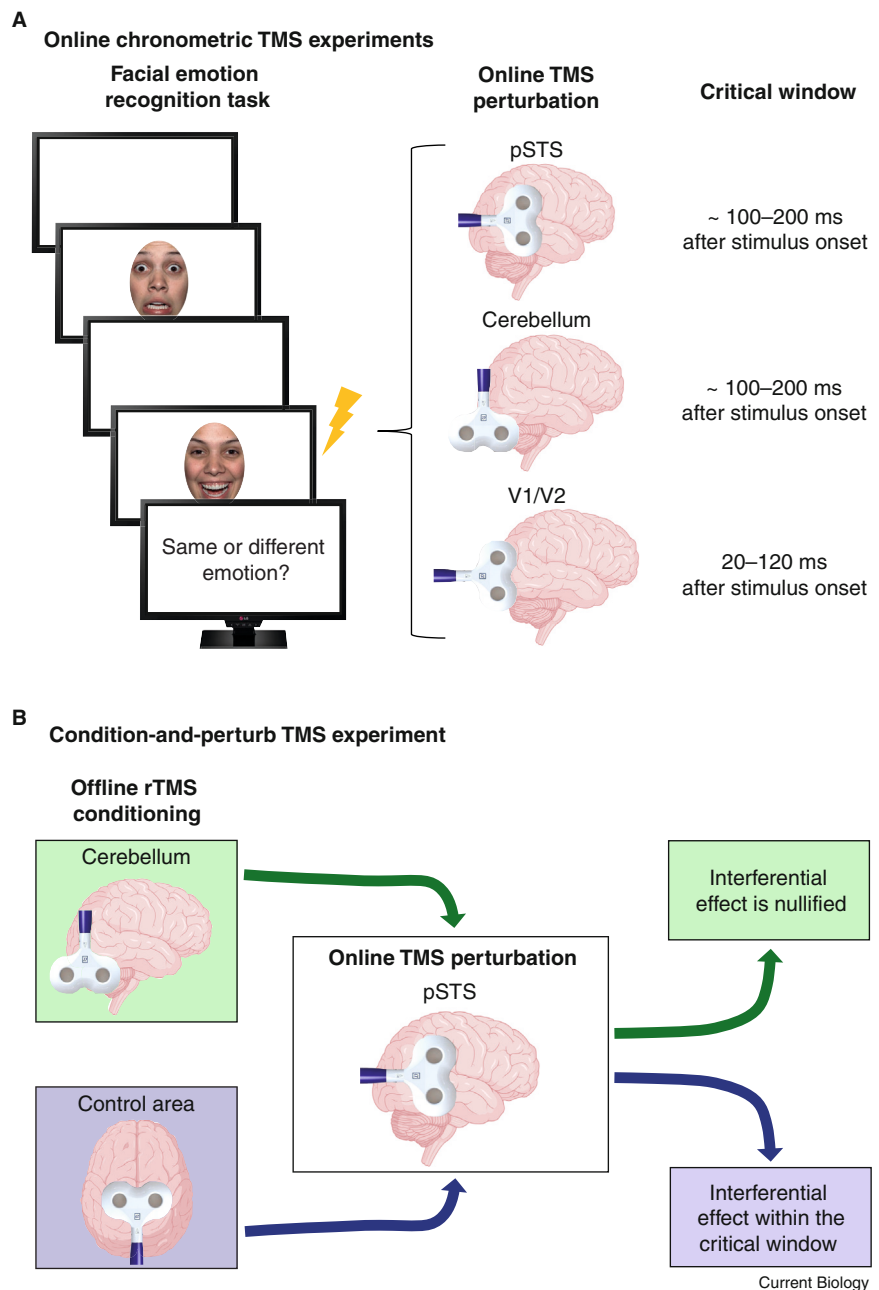
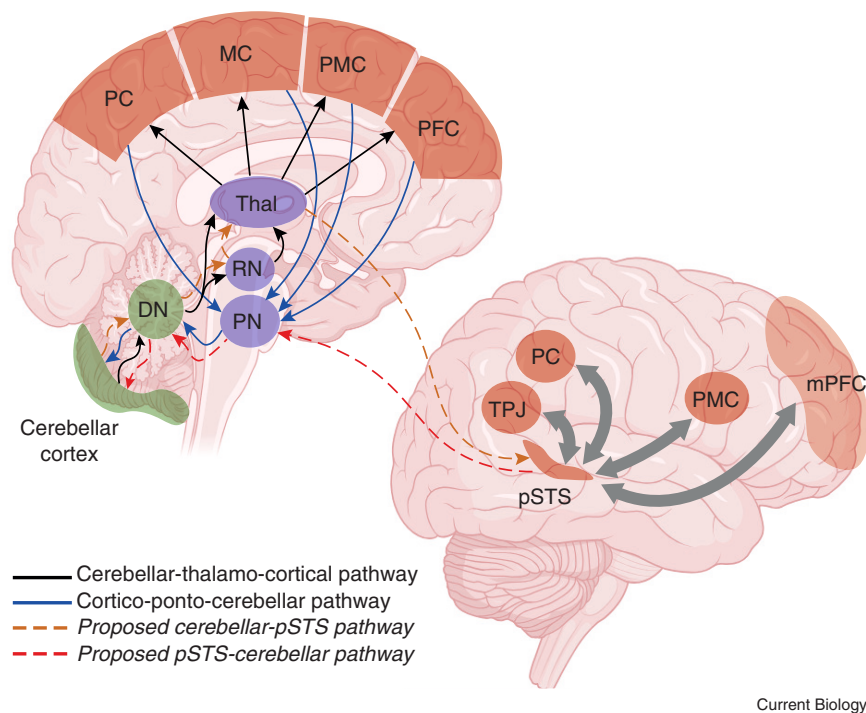


Figure 1. Main experimental conditions and results of Ciricugno *et al.*'s study.

(A) In the first two experiments, online TMS perturbation interfered with emotion recognition when administered over the posterior cerebellum or pSTS within a critical window of approximately 100–200 ms following the presentation of the second target stimulus in each trial. (B) To test the functional link between the two regions, in the third experiment, offline rTMS conditioning of the posterior cerebellum was applied; this manipulation effectively abolished the interference effect observed following online TMS over pSTS, suggesting this effect is dependent on cerebellar activity.

areas^{9,19} and sending bidirectional projections to premotor and parietal regions — thought to facilitate the perception of others' actions, facial expressions, and body language via sensorimotor resonance mechanisms — and high-order cortical nodes of the

mentalizing network such as the medial prefrontal cortex and the temporoparietal junction, involved in understanding and predicting mental states^{18,20}. Current evidence suggests that the cerebellum also plays a role in these processes^{4,5}. Extended analyses



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Figure 2. How the cerebellum crosses paths with the social brain.

Research on the role of the posterior cerebellum in social cognition has led scholars to search for anatomical connectivity between the cerebellum and the social brain. Alongside the classic cerebellar-thalamo-cortical and cortico-ponto-cerebellar tracts (blue solid)^{1,7}, a bi-directional cerebellar-temporal (dotted lines) pathway has been recently documented¹¹. Specifically, DTI evidence indicates the existence of a fiber bundle connecting the left posterior cerebellum to the right pSTS which, in turn, is a critical hub of the social brain, densely connected to all other major nodes of this network (grey arrows). Abbreviations: DN, dentate nucleus; PN, pontine nucleus; RN, red nucleus; Thal, thalamus; PC, parietal cortex; MC, motor cortex; PMC, premotor cortex; PFC, prefrontal cortex; TPJ, temporoparietal junction; pSTS, posterior superior temporal sulcus; dmPFC, dorsomedial prefrontal cortex.

of functional connectivity indicate that all these regions form function-specific cortical networks involved in sensorimotor resonance and mentalizing and are connected to function-specific subdivisions of the cerebellum^{7,10}.

If the posterior cerebellum and pSTS are functionally coupled, this still leaves an important question. How are these regions anatomically connected? Classical studies in primates have delineated two primary tracts linking the cerebellum with the cortex: the cortico-ponto-cerebellar tract and the cerebellar-thalamo-cortical tract, which together form a closed-loop system¹ (Figure 2, solid lines). According to these studies, cortical areas that project to and receive inputs from the cerebellum encompass the dorsolateral prefrontal, premotor, motor, and parietal regions, while direct connections with the temporal cortex seem absent, suggesting potential indirect cerebellar connectivity to pSTS

via fronto-parietal cortical projections (Figure 2, grey arrows). However, recent DTI evidence in humans has identified pathways connecting the left posterior cerebellum and the right pSTS, forming a bidirectional loop within the social brain¹¹ (Figure 2, dotted lines). This suggests the possibility of both direct and indirect communication routes between the posterior cerebellum and pSTS, potentially orchestrating the complex computations underlying social cognition.

Further neurophysiological investigations combining chronometric approaches with the conditioning of multiple regions^{14,15,19} are warranted to elucidate the functional properties of bidirectional cerebellar-cortical connections, including their potential for plasticity and their functional relevance to social perception. The results reported by Ciricugno, Ferrari *et al.* are a compelling new demonstration of this approach. Their study provides novel insights into the

functional role of the posterior cerebellum while opening up many exciting and important questions for future study.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Cell fusion: Inter-organ tissue communication promotes a union between myoblasts

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<https://doi.org/10.1016/j.cub.2024.03.048>

Repeated rounds of fusion between apposing myoblasts allow muscles to become multinucleated. New research finds that myoblasts undergoing fusion in the *Drosophila* embryo respond to hormone signaling from a nearby tissue, resulting in the activation of a myoblast-specific gene necessary for the fusion process.

The evolution of multicellular organisms gave rise to specialized and highly complex cell functions. Cells are separated by membranes, providing distinct environments for biochemical reactions and cellular functions. Sometimes, though, cells need to break down such barriers and mix their contents by fusing these membranes. For example, when a sperm joins with an oocyte, it starts a new life. In other cases, cell fusion is vital for the formation of multinucleated cells like skeletal muscle fibers, osteoclasts, and syncytiotrophoblasts in the placenta¹. These cells often require multiple nuclei to support their large size and specialized functions. Therefore, cell fusion is meticulously orchestrated to ensure efficiency and precision. New research by Ruan *et al.*² in a recent issue of *Current Biology* reveals that

inter-organ steroid hormone communication promotes myogenesis via direct transcriptional regulation of a key effector gene of muscle cell fusion.

The first ‘myoblast fusion’ genes were identified in unbiased mutagenesis screens performed in *Drosophila melanogaster* almost 30 years ago^{3–5}. Multiple laboratories have used similar approaches over the years to identify and characterize additional evolutionarily conserved genes required for this fusion process. In *Drosophila*, two distinct types of myoblasts are specified: unique founder cells serve as seeds for future muscles, and fusion competent myoblasts (FCMs) undergo repeated fusion events with founder cells to form syncytial myofibers. The cell adhesion molecule Dumbfounded (Duf) is expressed on the surface of

founder cells and forms a heterotypic complex with the transmembrane protein Sticks and Stones (Sns) on the surface of FCMs. At cell–cell contact sites mediated by Duf and Sns, downstream proteins, including F-actin, are recruited to the eventual fusion site. Final muscle size and nuclei number vary among the 30 different muscles within each abdominal hemisegment but form an invariant pattern by the end of myogenesis that ensures precise neural innervation and contractile properties for hatching and locomotion during larval life.

In a deficiency screen for new regulators of *Drosophila* embryonic myoblast fusion, Ruan *et al.*² pinpointed the *spook* (*spo*) gene. Like other members of the so-called ‘Halloween’ gene family, *spo* encodes an enzyme

