Developmental Neuroscience: How Twitches Make Sense

Animals refine the mechanics of their own bodies through sensorimotor feedback produced by physical interactions with the environment. A new study sheds light on how developing mammals may use sensations produced by spontaneous movements made during sleep to construct their sensorimotor maps.

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One fundamental difference that separates the living from the non-living is adaptability. Living organisms have an exceptional ability for fine-tuning their behaviors to the particular environment they inhabit. For example, we humans adapt our motor systems for walking, swimming, riding a bike, playing ball, a whole range of activities that even the most sophisticated machines find challenging, if not impossible. Organisms also must adapt to their ever-changing bodies and learn how to use them effectively to produce behaviors. In vertebrates, no time is more important in this regard than late fetal and early postnatal stages of development, when both the nervous system and body are changing radically and concurrently.

During early development, much of the interaction between the body and the brain is through self-generated movements — those movements that are not triggered by sensory input. Self-generated movements progress from having little or no discernable pattern and involving multiple body parts to more coordinated, discrete movement patterns and finally to flexible, adaptive movements. During this time, the connections between motor neurons and muscles go from being diffuse and non-specific to more selective, followed by the activity-dependent elaboration of new connections to the selected target muscle [1].

Very young animals, however, spend an inordinate amount of time sleeping, so how can there be enough 'activity' to guide this development of sensorimotor circuits? If you observe an infant animal sleeping — for example, a young squirrel, dog or human — you will notice that it frequently makes jerky movements, known as myoclonic twitches. In fact, a single muscle twitches hundreds of times in a 15 minute period of sleep [2]! Although to the casual eye these movements seem random, the twitches are actually structured [3], and there is increasing evidence that they aid sensorimotor development [4–7].

One of the big advantages of using sleep twitches as guides to sensorimotor development is that they are discrete movements in one part of the body, while the rest of the body is in a relaxed state with no muscle tension (atonia). In this physiological context, the sensory signals produced by twitches are highly salient to the developing nervous system — much more so than if the animal were awake and moving about. Against a background of high muscle tension and neural activity, it would be hard to resolve exactly which neural circuits should be linked to which muscles. In contrast, producing twitches against a background of muscle atonia enhances the signal-to-noise ratio and could, theoretically, be reliably used to determine how the twitching muscles relate to motor networks in the brain.

But there is a problem. Across the animal kingdom, organisms can distinguish between expected sensations arising from self-generated movements (like twitches) and unexpected sensations. They do so by sending a motor copy, known as a 'corollary discharge' or 'efference copy', of the movement signal to cancel the sensory signal that would otherwise arise from that movement [8,9]. This enables the animal to remain sensitive to unexpected sensory signals from the outside. Twitches are self-generated movements produced during sleep. If the sensory activity triggered by twitches is shut down, as in the case of awake self-generated movements, how can twitches be used as aids for developing sensorimotor circuits?

Tiriac *et al.* [10] addressed this puzzle head on by investigating the sensory-related neural activity generated by sleep twitches. The authors recorded proprioceptive sensory responses — those related to joints and tendons — in the hindlimb region of primary motor cortex (M1) of 8–10-day-old rat pups. As expected, when the pups were awake, self-generated hindlimb movements did not elicit any sensory-related activity, because such responses are squelched by motor copy signals. Conversely, passive movements of the limb by an experimenter while the pup was awake did elicit robust sensory responses. What sensory activity, if any, is elicited during sleep? Remarkably, self-generated movements during sleep — the twitches — did result in robust sensory-related neural activity, as did experimenter-initiated movements of the limb. Thus, twitches are processed as if they are unexpected movements and therefore elicit sensory activity that can be used to guide neural circuit development.

Critically, Tiriac *et al.* [10] pharmacologically activated lumbar-spinal neurons to produce movements (regardless of state) and the same sensory-related M1 activity was evident as it was for sleep twitches. That is, when the movement was initiated locally to the spinal cord, there was no canceling of the sensory signal. As the authors note, we currently do not know what neural circuits generate twitches in the first place, but their findings suggest two related hypotheses: first, that the source for generating sleep twitches is upstream of the spinal cord circuit (for example, in the forebrain or brainstem); and second, that this source may also generate the motor copy signal to cancel sensory responses in the awake state only.

Overall, the findings of Tiriac *et al.* [10] suggest that twitches are a special form of self-generated movement — they are treated as unexpected movements from the outside and the neural signal produced by these movements are, thus, not cancelled out. This being the case, they could be used to guide the development of sensorimotor neural circuits, but there is little direct evidence to date that twitches per se are necessary for the formation of sensorimotor maps in the brain.

Nevertheless, there are excellent theoretical frameworks that underscore the importance of twitches. Simulations and robotic platforms of limb muscles and associated neural connections have shown that twitches can induce the self-organization of sensorimotor circuits [11,12]. Of particular interest, Yamada and Kuniyoshi [12] simulated the integration of random spontaneous movements and the musculoskeletal systems of embryonic humans and fish within a prenatal environment. The foundation of their work rests on the principle that dynamic interactions within the body and brain, between the body and brain, and between the body and its environment drive the species-typical maturation of muscle and neural organization. In their simulations, each embryo 'developed' species-typical motor patterns without the need for any explicit instructions. Like the results of Tiriac *et al.* [10], these simulations underscore the importance of spontaneous movements like twitches during development: they are critical developmental processes that allow for adaptive and precise circuit construction without the need for a blueprint.

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