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Cracklin' Fish Brains

Whole-Brain Neuronal Activity Displays Crackling Noise Dynamics

Ponce-Alvarez A, Jouary A, Privat M, Deco G, Sumbre G. *Neuron*. 2018;100(6):1446-1459.e6. doi:10.1016/j.neuron.2018.10.045

Previous studies suggest that the brain operates at a critical point in which phases of order and disorder coexist, producing emergent patterned dynamics at all scales and optimizing several brain functions. Here, we combined light-sheet microscopy with GCaMP zebrafish larvae to study whole-brain dynamics in vivo at near single-cell resolution. We show that spontaneous activity propagates in the brain's 3-dimensional space, generating scale-invariant neuronal avalanches with time courses and recurrence times that exhibit statistical self-similarity at different magnitude, temporal, and frequency scales. This suggests that the nervous system operates close to a nonequilibrium phase transition, where a large repertoire of spatial, temporal, and interactive modes can be supported. Finally, we show that gap junctions contribute to the maintenance of criticality and that, during interactions with the environment (sensory inputs and self-generated behaviors), the system is transiently displaced to a more ordered regime, conceivably to limit the potential sensory representations and motor outcomes.

Commentary

The space in between is critical. Quite literally—in the physical sciences, we call it criticality. On one side, we find order and uniformity. On the other side, we find disorder and randomness. But at criticality—at the transition between order and disorder—interesting phenomena arise.

If a system is composed of many interacting parts, such as a nervous system composed of communicative neurons, then at the critical point we find local and dynamic pockets of order intermixed within disorder. Criticality has been observed in many physical systems and is well illustrated by the classic Ising model describing the directionality of spinning electrons within a magnet (eg, Figure 1A, and see the review by Sethna et al[1]). But can a physical relationship describing the behavior of a magnet also describe the behavior of the brain? Ponce-Alverez et al now provide compelling evidence that it can.

The authors of *Whole-Brain* Neuronal Activity Displays Crackling Noise Dynamics used calcium imaging techniques to evaluate the activity of neurons within the entire brain of a zebrafish and discovered that mesoscopic neuronal activity patterns follow several mandates dictated by criticality. Consistent with the concept of criticality, the authors observed many instances during which local clusters of spatially contiguous activity patterns generated by individual neurons transiently emerge and then disappear. As the dynamics of these clusters appear to follow those used to describe the concerted sliding of many sand grains down a pile of sand, these transient clusters of activity are called neuronal avalanches (Figure 1B and see the study by Beggs et al[2]). But clusters of ordered neuronal activity within a sea of disorder do not by themselves make criticality. Importantly, the authors demonstrate that several relationships among the neurons within the observed clusters follow the power law. And by demonstrating that power law relationships are followed in a system in which all constituents are monitored (eg, within the entirety of a single brain), the authors argue that the brain of a fish functions at criticality.

So, what is the power law? The law describes the relationship between 2 values in which one value varies as a power of the other value. The power law relationship can be illustrated with a simple example. Imagine a cube with a length of 10 meters. The volume of such a cube is 1000 meters^3. If we gradually decrement the cube's length by 1 meter, then the volume of the cube also decreases but not in a linear fashion. Instead, the cube's volume decreases exponentially, a relationship that is clearly observed when plotting length versus volume on a linear scale (Figure 1C, left). This relationship appears linear when plotted on a logarithmic scale (Figure 1C, right) and, in doing so, is said to follow a power law relationship.

Ponce-Alverez et al show that several features of neuronal avalanches observed in the zebrafish brain follow the power law. For example, the cumulative distributions of both the sizes and durations of neuronal avalanches are well described by a power law function (eg, Figure 1D). The relationship between

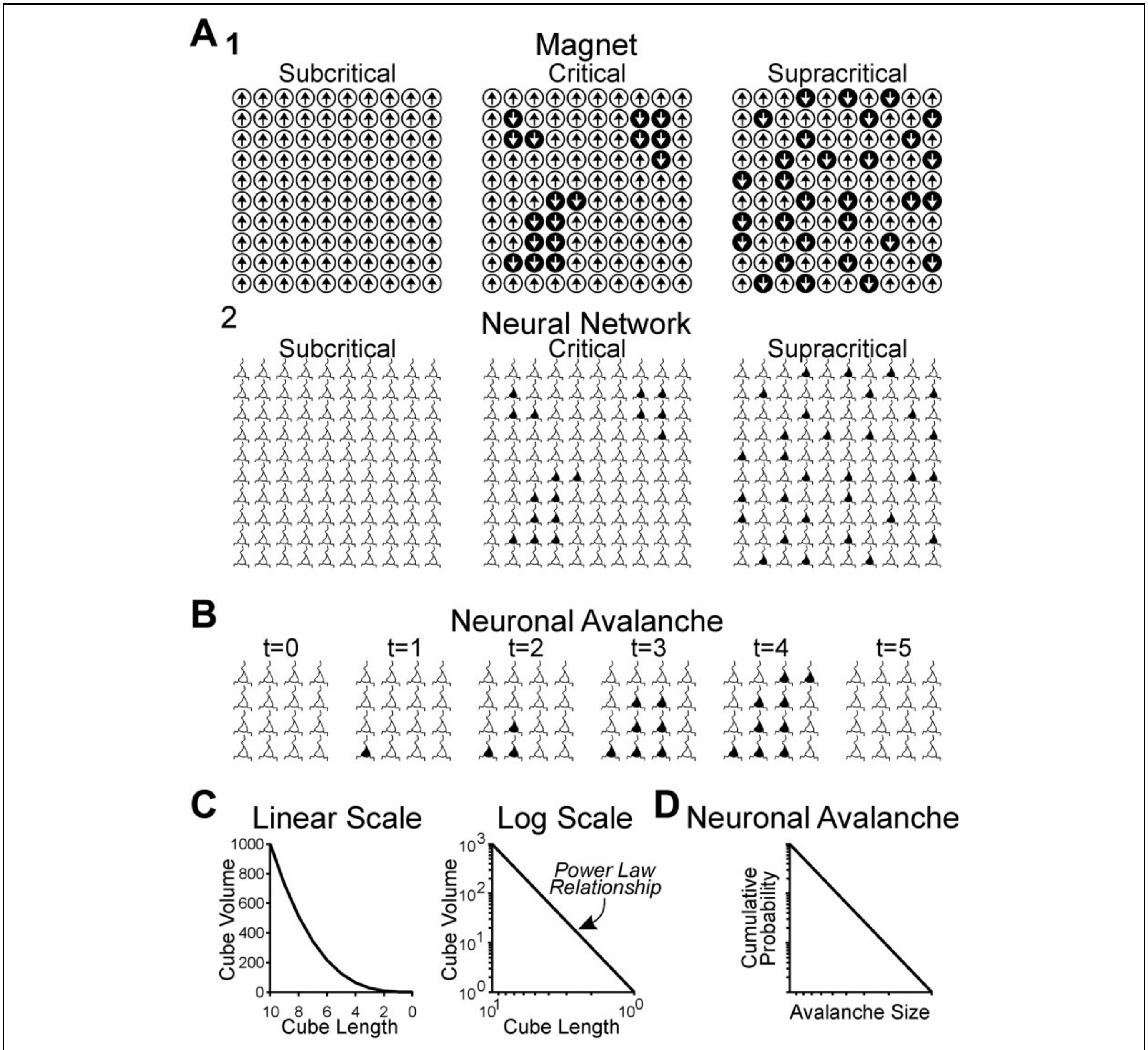

Figure 1. Neural activity patterns show signs of criticality. A, (1) Spinning of electrons within a magnet as described by the Ising model. The spinning of an electron is influenced by nearby electrons. At cooler temperatures (eg, left), such interactions dominate such that spin orientation is similar across all electrons within the magnet. If the temperature is raised (eg, right), then local electron interactions are disrupted and electron spins become random. At the critical temperature (eg, middle), local and dynamic clusters of spatially contiguous electrons with similar spin orientations emerge. Each circle represents an electron. Each arrow represents the orientation of the electron. (2) Schematic representing neural activity patterns operating at subcritical (left), critical (middle), and supracritical (right) regimes. Local clusters of spatially contiguous active neurons emerge at criticality. Active neurons are represented by filled cell bodies. B, Neuronal avalanche. A cluster of active neurons at different time points (*t*) transiently emerges and then disappears. The statistics of neuronal avalanches is similar to those observed during sandpile avalanches. C, Power law relationships plotted on linear (left) and log (right) scales. As an example, the volume of a cube is plotted as a function of the cube's length. This relationship appears linear when using a log scale. D, Ponce-Alverez et al (2) show that several features of neuronal avalanches recorded in the entire zebrafish brain follow the power law.

avalanche duration and avalanche size also follows the power law. Finally, irrespective of avalanche membership, the correlation of activity generated by 2 neurons in the zebrafish brain decays as a function of the Euclidian distance between them, a relationship that also follows the power law. Collectively, these power law relationships provide strong evidence that the zebrafish brain operates at the critical point. This conclusion is further strengthened by the observation that the neuronal avalanches can be well-described by a universal scaling function. That is, neuronal avalanche features are similar regardless of size (ie, are scale-invariant). Systems with these characteristics are said to crackle.[1] Zebrafish brain crackling, the authors finally show, depends on electrical synapses formed by gap junctions.

Many dynamical systems crackle, including the Earth and its earthquakes, the sounds associated with crumpling a piece of paper and, of course, fire.[1] But why is it significant for a brain to be characterized as a crackling system operating at criticality? One answer, of course, is that it reveals that well-described, relatively simple mathematical relationships may in fact be used to understand the incredibly complex neuronal activity patterns produced by the brain, a prosaic yet nonetheless reassuring conclusion (ie, there is hope). Perhaps a more meaningful answer, however, lies in the fact that systems operating within the critical regime are endowed with several functional advantages, as described in an excellent review by Shew and Plenz.[3] First, systems operating at criticality are characterized by the capacity to distinguish a large range of external stimuli [ie, high dynamic range[3,4]]. Second, such systems can transfer information with high capacity and fidelity.[5] In sum, both theoretical and experimental studies indicate that operating at criticality is good for the brain. To borrow a quote from Shew and Plenz[3]: "a healthy cortex is a well-balanced cortex". And a well-balanced cortex is one that operates at the transition between order and disorder.

If criticality is healthy, then what can be said of the epileptic brain? Emerging reports suggest that criticality breaks down during a seizure. To potentially understand why, it is important to recognize that criticality is set by, among other things, the connectivity among neurons within the brain. Beggs and Plenz[2] and Shew et al[5] demonstrated that reducing either excitatory or inhibitory transmission reduces the criticality of neural activity generated by cultured cortical preparations (ie, activity parameters deviate from the power law). Thus, it appears that appropriately balanced excitation and inhibition is important for a neural system to operate at criticality. Consistent with this hypothesis, the electrophysiological patterns recorded in tissue resected from pediatric patients with epilepsy, tissue that likely has an imbalance between excitation and inhibition, do not appear to operate at criticality despite producing bouts of elevated activity.[6] More recently, a similar conclusion was derived following analysis of seizures in patients (ie, in vivo[7]).

In conclusion, ample evidence now exists to indicate that the rules that govern magnets might be applied to the brain, as was proposed nearly 70 years ago.[8] By recording activity patterns within an entirely intact brain, Ponce-Alverez et al now provide more definitive proof. And if we can impose this theoretical construct on healthy and diseased brains, then perhaps experimentally testable predictions will follow. Future cracklings should enlighten.

By Mark P. Beenhakker

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