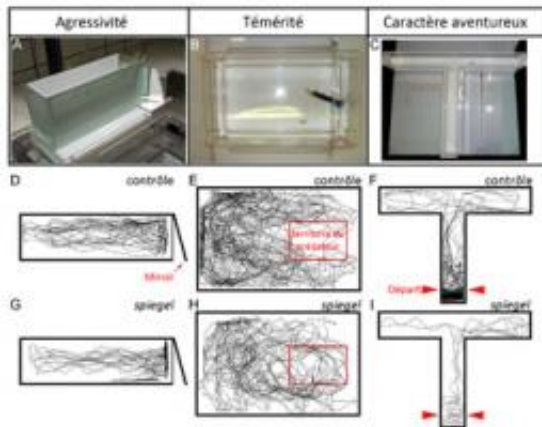


Aggression-boldness gene identified in model fish

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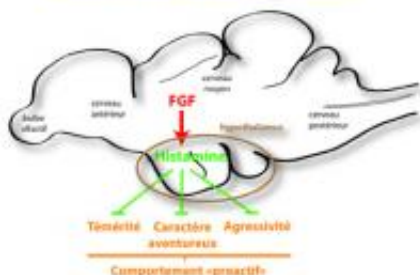


A-C: Principle of the behavioral tests used to measure the three facets of proactive behavior. A: The fish is placed in an aquarium with a mirror on one of its sides that reflects it. The fish does not recognize itself and attacks the “intruder”. B: The fish is placed in a neutral aquarium that contains a predator lure. The fish tends not to invade the predator's territory. C: The fish is placed at one end of a T-shaped aquarium. The time that it takes to leave this starting point and fully explore the arms of the T is measured. D-F: Paths followed by a control fish in these three tests (recorded by video). G-H: Paths followed by a spiegeldanio mutant fish. G: The time spent against the mirror is longer. H: The predator's territory is explored. I: The starting point is quickly left to explore the arms of the T. Credit: William Norton

A gene responsible for aggressive and bold behavior has been identified in zebrafish by a French team from CNRS/Laboratoire Neurobiologie et Développement. This specific behavioral association, whose three

characteristics are boldness, exploratory behavior and aggressiveness, has been described in many animal species. In zebrafish, it could be due to the action of a single gene (*fgfr-1*) through its regulation of histamine levels in the brain, as histamine is the neurotransmitter involved in numerous behavioral traits. These results are published in *The Journal of Neuroscience* on 28 September 2011.

The “Aggression-boldness syndrome” is well known to specialists. It is characterized by above-average boldness, exploratory behavior and aggressiveness. This syndrome, also known as proactive behavior, has been described in numerous species of fish, birds and mammals. Researchers from CNRS/Laboratoire Neurobiologie et Développement decided to study it in zebrafish, an animal model increasingly used by both geneticists and neurobiologists. They firstly developed behavioral tests so as to quantitatively measure the three facets of this aggressive and bold behavior. They then identified a strain of zebrafish, known as *spiegeldanio*, whose proactive nature clearly differs from the norm. Tests have shown that these fish are particularly aggressive towards their congeners, little intimidated by lures simulating predators and more adventurous in exploring new environments.



Top: Zebrafish Bottom: Schematic representation (showing a lateral view of the brain of the Zebrafish) of the genetic control of the three facets of proactive behavior by FGF signaling and the intermediate histamine neurotransmitter. A key area in the process is the hypothalamus (brown oval). Credit: Laure Bally-Cuif

The spiegelanio strain has a mutation in its *fgfr-1* gene coding for a membrane receptor sensitive to FGF, a growth factor that plays a key role in the development of vertebrates, particularly in brain growth. The mutation of the Fgfr1 receptor present in spiegelanio reduces the activation of the intracellular signals normally triggered by FGF. As a consequence of this mutation, spiegelanio fish exhibit low brain levels of histamine, a neurotransmitter known to regulate appetite, sleep and attention. These low histamine levels are responsible for the abnormal behavior of the zebrafish. In fact, a simple pharmacological treatment aimed at increasing histamine levels made fish with the spiegelanio mutation recover normal behavior, in other words average zebrafish behavior.

This work shows that the combination of the three characteristics defining aggressive and bold behavior depends on the action of a single gene present in all vertebrates. Environmental factors (physico-chemistry, animal density, food supply, etc.) are also likely to have an influence on behavior, but the *fgfr-1* gene seems to regulate the basic level of proactivity. These results shed light on this specific molecular and neurophysiological behavior. Nevertheless, further studies must be carried out to elucidate the molecular mechanisms that link the *fgfr-1* gene to histamine levels and the production of histamine to animal behavior.

More information: Modulation of Fgfr1a Signaling in Zebrafish Reveals a Genetic Basis for the Aggression–Boldness Syndrome. William H. J. Norton, et al. *The Journal of Neuroscience*, 28 September 2011.

Provided by CNRS

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