The influence of the menstrual cycle on the female brain

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What influence does the variation in estrogen level have on the activation of the female brain? Using functional Magnetic Resonance Imaging, Jean-Claude Dreher, a researcher at the Cognitive Neuroscience Center (CNRS/Université Lyon), in collaboration with an American team from the National Institute of Mental Health (Bethesda, Maryland) directed by Karen Berman, has identified, for the first time, the neural networks involved in processing reward-related functions modulated by female gonadal steroid hormones.

This result, which was published online on January 29, 2007 on the *PNAS* website, is an important step in better comprehension of certain psychiatric and neurological pathologies.

The human brain has a recompense system that predicts different types of reward (food, money, drugs…). The normal functioning of this system plays a fundamental role in many cognitive processes such as motivation and learning. This reward system, composed of dopaminergic neurons1 situated in the mesencephalon (a very deep region of the brain) and their projection sites, is crucial for neural coding of rewards. Its dysfunction can result in disorders such as addictions and is also implicated in various psychiatric and neurological pathologies, such as Parkinson's disease and schizophrenic disorders. Many studies on animals prove that the dopaminergic system is sensitive to gonadal steroid hormones (estrogen, progesterone).

For example, female rats self-administer cocaine (a drug that acts on the

dopamine system) in higher doses after estrogens have been administered to them. The influence of gonadal steroid hormones on the activation of the reward system remained to be studied in humans. A better knowledge of this influence should make for better understanding of the differences between men and women, particularly as observed in the prevalence of certain psychiatric pathologies and in vulnerability to drugs, (for which the dopaminergic system plays an important role.) It is known, for example, that the female response to cocaine is greater in the follicular phase of the menstrual cycle than in the luteal phase. Moreover, schizophrenia tends to appear later in women than in men.

1. Dopamine is a neurotransmitter, more specifically a molecule that modulates neuron activity in the brain. Dopaminergic neurons use dopamine as a neurotransmitter/neuromodulator.

2. Structures including the ventral striatum, the anterior cingulate cortex, and the orbitofrontal cortex.

3. Dopaminergic system: all the brain structures innervated by dopaminergic neurons.

4. Follicular phase: the first part of the menstrual cycle starting from the first day of the period.

5 Luteal phase: the second pat of the menstrual cycle that begins after ovulation and ends on the last day of the period.

6. Gonadal neurosteroids: steroidal hormones produced by the gonads (ovaries and testicles), which interact with estrogen receptors, progesterone or androgens.

7. Luteinizing hormone (LH) is a hormone produced by the pituitary gland. Its main role is to trigger ovulation, which occurs between 36 and

48 hours after the LH peak.

An increase in brain activity with anticipation of uncertain monetary rewards is observed. During the follicular phase, this is in the amygdala and the orbitofrontal cortex. (The higher the T values, the more the colors go from red to yellow, and the "statistically" higher the brain activity.)

Estrogens and progesterone are not just sex hormones that influence ovulation and reproduction; they also affect a large number of cognitive and affective functions.

These two observations show that gonadal neurosteroids modulate the female dopaminergic system, but the question remains as to whether these hormones modulate the reward system neuron network.

In order to answer this question, the team developed an experiment using functional Magnetic Resonance Imaging (fMRI). The brain activity of a group of women was examined twice during their menstrual cycle. Each time they went into the MRI, they were presented with virtual slot machines showing different probabilities of winning. When women anticipate uncertain rewards, they activate the brain regions involved in processing emotions, particularly the amygdala and the orbitofrontal cortex, to a greater extent during the follicular phase (4 to 8 days after the start of the period) than during the luteal phase (6 to 10 after the LH hormone surge). These results demonstrate increased reactivity of the female recompense system during the follicular phase, which is also the phase in which the estrogens do not oppose the progesterone. In order to determine the gender-related differences of reward system activation, the same experiment was carried out on a male group. Result: when men anticipate rewards, they mainly activate a region involved in motivation for obtaining rewards, the ventral striatum, whereas in women, it is a region dealing with emotions, the amygdalo-hippocampal region, which

is the most highly activated.

These conclusions could be applied to rewards other than monetary. Take receptiveness and desire, for example, two qualities that are supposed to facilitate procreation and are seen during the period of ovulation. It could be envisaged that the increase in activity of certain regions of the female brain during the follicular phase would modulate behavior linked to obtaining rewards, such as approach behavior during reward anticipation and hedonistic behavior when the reward is received.

These results, at the border between neuroendocrinology and neurosciences, provide a better understanding of the fundamental role of gonadal steroid hormones on reward processing, particularly in behavioral processes such as motivation and learning. They also important in understanding the dysfunction of the reward system observed particularly in cases of Parkinson's disease, schizophrenia, normal ageing and drug and gambling addictions.

Source: CNRS