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The molecular mechanisms of sexual orientation and gender identity

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1 **Title: The molecular mechanisms of sexual orientation and gender identity**

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3 **Running title:** Sexual orientation and gender identity

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5 **Key words:** Sexual orientation, gender identity, brain, hormones, genetic

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7 **Abstract:**

8 Differences between males and females are widely represented in nature. There are gender
9 differences in phenotypes, personality traits, behaviors and interests, cognitive performance, and
10 proneness to specific diseases. The most marked difference in humans is represented by sexual
11 orientation and core gender identity, the origins of which are still controversial and far from being
12 understood. Debates continue on whether sexual behavior and gender identity are a result of
13 biological (nature) or cultural (nurture) factors, with biology possibly playing a major role. The
14 main goal of this review is to summarize the studies available to date on the biological factors
15 involved in the development of both sexual orientation and gender identity. A systematic
16 search of published evidence was performed using Medline (from January, 1948 to June, 2017).
17 Review of the relevant literature was based on authors' expertise. Indeed, different studies have
18 documented the possible role and interaction of neuroanatomic, hormonal and genetic factors. The
19 sexual dimorphic brain is considered the anatomical substrate of psychosexual development, on
20 which genes and gonadal hormones may have a shaping effect. In particular, growing evidence
21 shows that prenatal and pubertal sex hormones permanently affect human behavior. In addition,
22 heritability studies have demonstrated a role of genetic components. However, a convincing
23 candidate gene has not been identified. Future studies (e.i. genome wide studies) are needed to
24 better clarify the complex interaction between genes, anatomy and hormonal influences on
25 psychosexual development.

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28 **1. Introduction**

29 Differences between the two sexes are widely represented in nature. Even among humans, males
30 and females differ in many aspects: biological phenotypes (Luders et al., 2009; Ngun et al., 2011),
31 personality traits (Luders et al., 2009; Ngun et al., 2011; Collazzoni et al., 2017), behaviors and
32 interests, cognitive performance and proneness to specific diseases (Berenbaum and Beltz, 2011). In
33 the last few decades, science has focused on understanding the origins of such differences, in
34 particular the specific influence and shaping role of genes, hormones, environment and/or

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