Evidence from previous studies has reported that complex traits, including psychiatric disorders, are moderately to highly heritable. Moreover, it has also been shown that specific personality traits may increase the risk to develop mental illnesses. Therefore the focus of the research shifted towards the identification of the biological mechanisms underpinning these traits by exploring the effects of a constellation of genetic polymorphisms in healthy subjects. Indeed, studying the effect of genetic variants in normal personality provides a unique means for identifying candidate genes which may increase the risk for psychiatric disorders. In this review, we discuss the impact of two of the most frequently studied genetic polymorphisms on personality in healthy subjects, the 5-HTT polymorphism of the serotonin transporter and the DRD2/DRD4 polymorphisms of the D2/D4 dopamine receptors. The main aims are: (a) to highlight that the study of candidate genes provides a fruitful ground for the identification of the biological underpinnings of personality without, though, reaching a general consensus about the strength of this relationship; and (b) to outline that the research in personality genetics should be expanded to provide a clearer picture of the heritability of personality traits.

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Cooperativeness and Self-Transcendence. Cloninger with the 'Seeking and with the effect of the (1) dopamine, linked to Novelty behaviour. So far, the research in this field explored the effect of the (1) dopamine, linked to Novelty Seeking and with the 'system of behavioural activation'; (2) serotonin, related to Harm Avoidance and with the 'system of behavioural inhibition'; and (3) noradrenalin, associated with Reward Dependence (Comings et al. 2000). The majority of personality genetics studies based their investigation on the impact of genetic polymorphisms known to regulate the action of serotonin transporter (5-HTT) and dopamine’s receptors (DRD2 and DRD4) in both patients and healthy subjects. Therefore, we here specifically focus on serotonin and dopamine.

The 5-HTT is a functional polymorphism within the promoter sequence of the serotonin transporter gene and it is involved in a variety of processes, including impulsivity, suicidal ideation, mood and anxiety. Moreover, the presence of the short allele of this polymorphism (s-allele) was associated with major depression, anxiety and schizophrenia (Kuzelova et al. 2010). Similarly, the DRD2 and DRD4 are functional polymorphisms that regulate the expression of the dopamine D2 and D4 receptors, which are important in modulating reward, locomotion and learning. The low-frequent alleles within these polymorphisms are also linked to schizophrenia, depression and drug addiction (Missale et al. 1998). However, although the effects of these genes on psychopathology have been explored, there is not a general consensus about the strength and nature of the relationship between the serotonin and dopamine activity and personality traits in healthy subjects.

The importance of studying the role of genetic variants on human personality is evident especially because it might inform us on the traits that are more predictive of risk of psychiatric illnesses. With regard to the 5-HTT polymorphism, the majority of the studies on healthy subjects found significant associations with anxiety-traits, such as Harm Avoidance (Van Gestel & Van Broeckhoven, 2003). These findings are in line with the neurobiological basis of depression and anxiety which has been linked to the mechanism of action of serotonergic antidepressant medications. The first study that paved the way for the identification of the association between serotonin and personality traits was published in 1996 by Lesch et al. showing that carriers of the short allele of the 5-HTT polymorphism had higher Harm Avoidance. On the other hand, the DRD2 and DRD4 polymorphisms have been found to be associated with Novelty Seeking, which is linked with exploratory excitability and impulsivity (Ebstein et al. 1996; Noble et al. 1998) (see Table 1 for a selection of studies exploring the association between the serotonin and dopamine neurotransmitters and personality). This association is consistent with previous findings which reported the role of the dopamine in mediating exploratory behaviours in animal models as well as in emotion and cognition (Benjamin et al. 1996).

Interestingly, a recent review also reported a significant association between dopamine and the schizophrenia spectrum, including the schizotypal personality disorder (Mohr & Ettinger, 2014). This evidence further supports the importance of exploring the neurobiological bases not only of severe chronic disorders, but also of psychiatric spectra which include personality disorders as well as subjects with increased genetic and clinical risk for a specific illness. However, it is important to highlight the existence of some negative studies which found no association with these personality dimensions (Herbst et al. 2000; Gebhardt et al. 2004) as well as studies reporting contrasting results, with the same genetic variant associated with higher and lower scores in the same personality scale (van Gestel & Van Broeckhoven, 2003). In addition, there is increase evidence of the association between the 5-HTT and DRD2/DRD4 polymorphisms with character dimensions which, according to Cloninger’s Theory, are acquired during the development through socio-cultural learning and not as genetically determined as the temperament dimensions (Cloninger et al. 1994). Studies from different cultural populations reported that healthy subjects carriers of the short allele within the 5-HTT showed lower scores in all the Cloninger’s character dimensions, including Self-Transcendence (Ham et al. 2004), Self-Directedness (Gonda et al. 2009; Saiz et al. 2010; Calati et al. 2014) and Cooperativeness (Pelka-Wysiecka et al. 2012). Similarly, for the DRD2 polymorphism, Tsuchimine et al. (2012) found that the less frequent allele was associated with significant lower scores in the Self-Directedness scale (Table 1). This biological evidence further supports the findings from independent twin studies, which supported a similar heritability for temperament and character dimensions (Al-Halabi et al. 2011; Brambilla et al. 2014; Picardi et al. 2015).

In conclusion, these findings point to two new avenues of enquiry in relation to personality traits. First,
the results from the personality genetics studies, together with previous evidence from family and twin studies reporting heritability estimates of personality traits, further suggest that genes play a greater role in shaping all aspects of personality, including both character and temperament dimensions. Second, although the study of specific candidate genes brought compelling findings, the lack of consistency underscores the need for a more detailed examination of the role of genetic variants on personality traits. Indeed, the success of the future genetics personality research in identifying genetic factors might be linked to (a) the employment of larger sample size which may overcome the limitations of the current studies characterised by small sample size and therefore with low explanatory power; (b) the investigation of multiple genetic variants, especially because complex traits are characterised by pleiotropy and polygeneity (Plomin et al. & Deary, 2015); and (c) the differentiation of the sample according to the age and sex of the participants which have been reported to significantly influence personality scales (Fresán et al. 2011).

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### Conflict of Interest

None.

### Ethical Standard

The authors declare that no human or animal experimentation was conducted for this work.

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