The association between the serotonin and dopamine neurotransmitters and personality traits

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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’s 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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The investigation of the biological bases of personality has been an object of study for a long time. Specifically, inter-individual variations in personality traits have been considered highly heritable and therefore associated with the action of specific neurotransmitters which are, in turn, regulated by a biological constellation of genes and their polymorphic variants (Cloninger et al. 1994). Although there is a variety of questionnaires used for exploring the personality’s profile of individuals, the Temperament and Character Inventory (Cloninger et al. 1994) is the most widely used and validated scale employed for identifying the biological underpinning of personality traits.
(Comings et al. 2000; Brändström et al. 2001). This psychobiological model of personality identified seven clusters that can be subdivided in four dimensions of temperament – Harm Avoidance, Novelty Seeking, Reward Dependence and Persistence – and three dimensions of character – Self-Directedness, Cooperativeness and Self-Transcendence. Cloninger’s theory of the inter-relation between neurotransmitters and personality traits has opened a new field of investigation exploring the impact of specific genetic polymorphisms on personality and therefore on human 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) noradrenaline, 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, here we 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.

References

Table 1. Selection of studies investigating the association between serotonin and dopamine neurotransmitters and personality in healthy subjects

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of subjects</th>
<th>Polymorphism</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesch et al. (1996)</td>
<td>505</td>
<td>5-HTT</td>
<td>5-HTT (s-allele) associated with higher Harm Avoidance</td>
</tr>
<tr>
<td>Herbst et al. (2000)</td>
<td>587</td>
<td>5-HTT</td>
<td>No association between 5-HTT and Harm-Avoidance</td>
</tr>
<tr>
<td>Ham et al. (2004)</td>
<td>147</td>
<td>5-HTT</td>
<td>5-HTT polymorphisms associated with Self-Transcendence</td>
</tr>
<tr>
<td>Gonda et al. (2009)</td>
<td>169</td>
<td>5-HTT</td>
<td>5-HTT (s-allele) associated with lower Self-Directedness</td>
</tr>
<tr>
<td>Saiz et al. (2010)</td>
<td>404</td>
<td>5-HTT</td>
<td>5-HTT (s-allele) associated with lower Self-Directedness</td>
</tr>
<tr>
<td>Peóka-Wysiecka et al. (2012)</td>
<td>406</td>
<td>5-HTT</td>
<td>5-HTT (s-allele) associated with lower Cooperativeness</td>
</tr>
<tr>
<td>Dopamine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ono et al. (1997)</td>
<td>153</td>
<td>DRD4</td>
<td>Long alleles of the polymorphic exon III repeat sequence of DRD4 associated with Novelty Seeking</td>
</tr>
<tr>
<td>Noble et al. (1998)</td>
<td>119</td>
<td>DRD2</td>
<td>DRD2 less frequent allele associated with higher Novelty Seeking</td>
</tr>
<tr>
<td>Gebhardt et al. (2004)</td>
<td>109</td>
<td>DRD2, DRD4</td>
<td>No significant association of DRD2 and DRD4 genes with personality traits</td>
</tr>
<tr>
<td>Lee et al. (2003)</td>
<td>243</td>
<td>DRD4, DRD2</td>
<td>DRD4 gene associated with Novelty Seeking in females. Females with DRD2 less frequent alleles (-141C Ins/Ins genotype) associated with higher Reward Dependence</td>
</tr>
<tr>
<td>Tsuchimine et al. (2012)</td>
<td>1084</td>
<td>DRD2</td>
<td>DRD2 gene associated with Self-Directedness. Men with less frequent allele (-141C Ins/Ins Del/Ins genotype) associated with lower Self-Directedness compared to males with -141C Ins/Del alleles.</td>
</tr>
</tbody>
</table>


