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Effect of Genetic predispositions, Caregiving propensities and Culture on In-person and Online Social Attitudes

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To my dad

Abstract

Humans are inherently social creatures. Affiliative and social behaviours evolutionarily facilitate cooperation with the conspecifics to increase adaptation and ensure the species' survival. Nature and nurture have a programming effect on the trajectories of human social development. Specifically, genetic and environmental mechanisms shape social bonds from infancy to adulthood. Early caregiving also has a pivotal role in social development among the early environmental influences. Sensitive caregivers respond efficaciously to an infant's physiological and affective needs and promote a high-quality parent-infant relationship. A secure and positive attachment in childhood has a longitudinal impact on adult relationships. Within the genetic and epigenetic frameworks, research points to the implication of the Oxytocin Receptor Gene (*OXTR*) and the Serotonin Transporter Gene in moderating caregivers' influences over social behaviour. However, how such factors are involved in dynamic interaction to forge social bonds is almost undefined.

The current research probes if early caregiving, adult attachment, genetic predispositions and cultural factors can predict adult sociability. This multidisciplinary and cross-cultural project covers the topic of over nine studies that explore the intersection among genes, culture, neural correlates, caregiving behaviour, affiliative propensities and in-person and online social behaviour. More precisely, the current work is a compendium of three pieces of research that target the effect of *OXTR* polymorphisms and parental bonding or adult attachment on adult social attitudes. In a first study, we investigated the effects of the genetic susceptibility of *OXTR* rs53576 and early parental bonding on the levels of anxiety and avoidance experienced in romantic relationships across two different cultural contexts, namely Italy and Singapore. In a second study, we inspected the effects of the genetic variations of *OXTR* (rs53576; rs2254298) and caregiving propensities on the levels of online sociability on a social network site, such as Instagram, in a cultural con-

text highly sensitive to technologies. In a third study, we explored the effects of the same genetic factors and adult attachment dimensions from romantic relationships on the frequency of Instagram sociability in the same cultural context. Related and secondary studies of the research project are cited and briefly discussed.

In the field of developmental psychobiology, the results fit a) the Prototype Hypothesis, which assumes that infant attachment representations are reproduced in adult social relationships; and b) the Differential-Susceptibility and Resilience Hypothesis which postulated the difference between plastic genes more susceptible to environmental modifications and non-plastic genes highly resilient to adverse conditions. Considering the overall findings and starting from the Bioecological Model of development, a theoretical model is advanced to integrate the numerous predictors of social behaviour into a coherent architecture. Whereas cultural and genetic mechanisms are mainly fixed, early caregiving adjusts the long-term trajectory of social development. Moreover, in-person peer and close relationships, as well as online user-to-user relationships are not merely developmental outcomes. They are also social regulators that can adjust to the social responses in adult life.

Disclaimer

The whole research project is formed by the following nine studies (**1, 2, 3, A, B, C, D, E, F**). As part of the project, the current doctoral thesis presents these studies following a specific structure. Chapters 2, 3 and 4 are based on published studies 1, 2 and 3. Chapter 5 is partly based on studies 1, 2 3 and briefly discusses the secondary studies A, B, C, D, E, F within a unique scenario. Table 1 summarizes the structure of the thesis and describes the included content (original or from existing publications).

Structure of the Thesis

Section	**Content**
Abstract	Original
Chapter 1	Original
Chapter 2	Based on Study 1 with minor variations
Chapter 3	Based on Study 2 with minor variations
Chapter 4	Based on Study 3 with minor variations
Chapter 5	Based on Studies 1, 2, 3, A, B, C, D, E, F with original additions

Table 1: Summary of the thesis structure and use of the content. The content of this work is original or based on existing publications.

Study 1. Cataldo, I., Bonassi, A., Lepri, B., Foo, J. N., Setoh, P., Esposito, G. (2021). Recalled parental bonding interacts with oxytocin receptor gene polymorphism in modulating anxiety and avoidance in adult relationships. *Brain sciences*, 11(4), 496. DOI: 10.3390/brainsci11040496.

Study 2. Bonassi, A., Cataldo, I., Gabrieli, G., Foo, J. N., Lepri, B., Esposito, G. (2020). Oxytocin receptor gene polymorphisms and early parental bonding interact in shaping Instagram social behavior. *International journal of environmental research and public health*, 17(19), 7232. DOI: 10.3390/ijerph17197232. Preregistration: https://osf.io/j9nqc.

Study 3. Carollo, A., Bonassi, A., Cataldo, I., Gabrieli, G., Tandiono, M., Foo, J. N., Lepri B., Esposito, G. (2021). The relation between

Oxytocin Receptor Gene polymorphisms, adult attachment and Instagram sociability: An exploratory analysis. *Heliyon*, 7(9), e07894. DOI: 10.1016/j.heliyon.2021.e07894. Preregistration: https://osf.io/t78fu.

Study A. Bonassi A., Cataldo I., Gabrieli G., Lepri B., Esposito G. (2021). Serotonin Transporter Gene Polymorphisms and Maternal Overprotection Regulate Adult Social Expectations on Close Relationships. *Brain sciences* 11(4), 496. DOI: 10.3390/brainsci11091123.

Study B. Bonassi A., Cataldo I., Tandiono M., Foo J.N., Lepri B., Esposito G. (2021). Effect of early paternal caregiving and genotype rs25531 polymorphisms on the adult relationship with the partner. *European Neuropsychopharmacology* 44(6), S9-S10. DOI: 10.1016/j.euroneuro.2021.01.019.

Study C. Bonassi, A., Cataldo, I., Tandiono, M., Foo, J. N., Lepri, B., Esposito, G. (2021). Genotype rs25531 polymorphisms and quality in peer relationships adjust the neural response of the anterior prefrontal cortex to cry. European Neuropsychopharmacology, 53, S380-S381. DOI: 10.1016/j.euroneuro.2021.10.488.

Study D. Bonassi, A., Cataldo, I., Gabrieli, G., Tandiono, M., Foo, J. N., Lepri, B., Esposito, G. (2020). The interaction between serotonin transporter allelic variation and maternal care modulates sociability on Instagram. *PsyArXiv.* DOI: 10.31234/osf.io/dkvnf.

Study E. Bonassi, A., Carollo, A., Cataldo, I., Gabrieli, G., Tandiono, M., Foo, J. N., Lepri B., Esposito, G. (2021). Modulation of Instagram Number of Followings by Avoidance in Close Relationships in Young Adults Under a Gene x Environment Perspective. *International journal of environmental research and public health*, 18(14), 7547. DOI: 10.3390/ijerph18147547.

Study F. Bonassi, A., Cataldo, I., Giulio, G., Foo, J. N., Lepri, B., Gianluca, E. (2020). Serotonin transporter gene polymorphisms and confidence in adult relationships affect the number of followed people on Instagram. *European Neuropsychopharmacology* 40(1), S385-S386. DOI: 10.1016/j.euroneuro.2020.09.500. Preregistration: https://osf.io/wxkq9

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Chapter 1

The origin of human social relationships

1.1 Humans are social: the role of sociability across the lifespan

Sociability is an innate and natural attitude of human cognition and behaviour. This term refers to the quality of being sociable with others based on the expression of individual social traits and characteristics. From the origin of the species, social abilities allow humans to cooperate with conspecifics to enhance the chance of survival (Richerson et al., 2003; Sussman and Cloninger, 2011). In the evolutionary viewpoint of fitness interdependence, the tendency to be social and cooperative in affiliative societies results from a mutual dependence that increases the chance of reproduction (Aktipis et al., 2018). For instance, human mating relationship assumes that partners can a) rely on each other, b) share benefits and risks to maximize the welfare of the couple, and c) have offspring together to keep a high reproductive success (Aktipis et al., 2018). Overall, humans are inclined to be social in gratifying psychological demands as well as physiological needs (McLeod, 2007; Baumeister, 2011). Newborns exhibit an innate preference towards social stimuli such as human faces. The exact requests for care, protection and support arise from the impulse to promote social ties (Royle et al., 2012).

Several theories have explored how social traits evolve across the lifespan. According to the Five-Factor Theory, sociability is a dimension of personality that develops during childhood and remains approximately stable across adulthood (McCrae and Costa Jr, 2008). In comparison, the Social Cognitive Theory conceives sociability as the individual and flexible cognitive strategy to adapt more efficiently to different contexts (Bandura, 1999). Only the modern Neosocioanalytic Theory combines continuous abilities (e.g., be prosocial and open to others) and dynamic processes resulting from changes that may occur with the advent of novel social experiences (e.g., be involved in new relationships, be the member of communities) (Roberts and Nickel, 2017).

Fewer researches focused on the trend of sociability across time. Recently, Brook and Schmidt (2020) traced the mean levels of sociability among age groups, observing that sociability follows a quadratic distribution across the lifespan. Specifically, the authors reported a universal downward trend from infancy to adulthood and a slight upward trend close to old age. Interestingly, the authors also found that no gender differences were present in childhood, while males socialize less than females in adulthood. Relative individual differences were described by Ashton and Lee (2016) or Crocetti et al. (2019).

1.2 The Early Environment: the lifelong impact of caregiving practices on social development

Multiple factors contribute to the development of social skills. Among all factors, parental influences play a crucial role in the flourishing of social competencies during infancy and childhood (Semrud-Clikeman, 2007; Esposito et al., 2017c). Family represents the first social environment where the infant freely plays and socially interacts with parents (Ginsburg et al., 2007). The parental bond finds its biological origin from an evolutionary co-regulation of physiological and endocrine mechanisms among mother, father, and baby (Feldman, 2007; Esposito et al., 2013). Recent research on parent-infant synchrony has witnessed different coordinated patterns of dyadic interaction at a cognitive, emotional, and social level (Azhari et al., 2019; Wass et al., 2020; Nguyen et al., 2020).

Parents are the main social agents able to foster the development of their baby's social abilities during several sensitive periods (Ainsworth et al., 1974). During a sensitive period such as infancy and childhood, the offspring acquires a wide range of knowledge in the world (e.g., object permanence, complex play, fluid conservation, symbolical thinking) and rapidly learn multiple skills (e.g., sensory, motor, linguistic) (see the American Psychiatry Association dictionary of psychology, for instance, VandenBos (2007)). Otherwise, the same abilities would be learnt with delay and difficulty outside this chronological window of opportunity (Gabard-Durnam and McLaughlin, 2019). Infancy may also be a period more susceptible to maltreatment or caregiving deprivation (Gee, 2020). According to the Sensitive Period Model, both favourable and adverse experiences may show long-term consequences (Bornstein, 2014; Orth, 2018). The first year of life is commonly recognized as the experience-dependent attachment period between the baby and the caregivers.

The Attachment Theory postulated by Bowlby (1973) asserts that attachment is the child's first social relationship with a specific formation, patterns, and lifelong implications. This psychological construct, common among mammalian species, is based on the biologically-founded desire for proximity (Harlow and Zimmermann, 1958; Bowlby, 1982; Cascio et al., 2019). In line with natural selection, higher proximity to the caregiver guarantees better protection and a higher probability of survival. The pup or baby activates different attachment behaviours (e.g., crying, smiling, following, clinging) to attract the attention of the mother and trigger her response of support and care (Esposito et al., 2015). Human attachment is, therefore: a) highly specific and b) enduring (the social bond between caregiver and infant); c) emotionally meaningful (characterized by affective and caring behaviours); looks for proximity (affiliative strategies satisfy needs and defence against danger); e) allows the infant to be feel secured and comforted. The promptness and efficacy of caregivers' reactions generate specific internal working models in the infant that are useful to predict actions, keep caregivers close, and make representations of the social interaction (Bretherton and Munholland, 2008; Truzzi, 2019). As attachment figures, parents offer a secure base from which the infant explores the world and preserve a safe haven where the infant returns to be protected (Marvin et al., 2002).

Although the formation of attachment is universal, the quality of each bond is individual and varies as a function of the caregiver and the relationship type. Starting from Bowlby's framework, Ainsworth (1978) conducted different observational studies using the Strange Situation Procedure to classify human attachment (Ainsworth et al., 1981). The observations revealed that every attachment style was characterized by peculiar behavioural patterns (Ainsworth et al., 2015). In conditions of secure attachment, the infant freely explores the environment, and the mother provides appropriate care and contact. An insecure attachment style instead highlights altered behavioural patterns. In the case of avoidant attachment, the mother is mostly unavailable, and the infant minimizes contact because he/she feels rejected (high feeling of abandonment). In the case of resistant attachment, the infant maximizes the behaviour to be sure that the mother will be present (high levels of anxiety). More problematic is the disorganized attachment, often the result of neglect or abuse, since the infant cannot predict how the mother will behave (Main et al., 1990).

Caregiving practices are directly linked to the construct of attachment. Parental sensitivity is a considerable predictor of attachment security. A sensitive mother is aware of the infant's cues and responds accurately and promptly to them. Behavioural responses such as breastfeeding, touch, and maternal social support are considered positive caregiving practices. Caregiving strategies are overall associated with emotional (Fearon et al., 2010; Groh et al., 2012), social (Groh et al., 2014), behavioural (Narvaez et al., 2013), physiological (Johnson et al., 2018), and neural outcomes

(Carollo et al., 2021c).

Positive caregiving practices enhance the early attachment with parents and lead to improved self-esteem, self-regulation, empathy, prosocial behaviour, and a higher propensity to undertake social relationships throughout human development (Bretherton, 1985; Canetti et al., 1997; Calkins and Leerkes, 2004; Laible et al., 2004; Rilling and Young, 2014). Toddlers with responsive mothers also show higher scores in executive functioning and proficient academic performance (West et al., 2013; Bernier et al., 2015). A supportive child-centred environment lays the groundwork for high-quality stimulation (exogenous environment) (Tucker-Drob and Harden, 2012). At the same time, children with skilled cognitive, linguistic, and social abilities enrich the same home learning environment (endogenous environment) (Bornstein, 1985; Camilli et al., 2010; Bornstein et al., 2020). This bidirectional process can be strengthened by a rewarding relationship with the parents, which promotes a focused and sensitive social education from childhood to adolescence (Camilli et al., 2010; Padilla-Walker et al., 2012).

Conversely, low-quality caregiving behaviour undermines social competence and cognitive performance during short and long term of development (Network, 2002; Beach et al., 2005). A history of familiar maltreatment is associated with cognitive delay, educational abandonment and renders people more vulnerable to further adversities (Romano et al., 2015). Emotional abuse and neglect can exacerbate more severe internalizing problems and health outcomes than physical or sexual abuse, such as psychiatric disorders (i.e. anxiety, mood, psychotic, personality and addiction disorders) (Strathearn et al., 2020). An antagonistic relationship with parents induces higher psychological and physiological distress, as well as negative emotionality (Gaggero et al., 2020) and attenuated capacity to cope with challenges (Crockenberg and Leerkes, 2003; Willinger et al., 2005; Thorberg et al., 2011; McLaughlin et al., 2015). Research in psychopathology highlight that babies become more sensitive to low care of anxious mothers expressing a differential self-comforting behaviour depending on gender and age (Müller et al., 2016). On the other hand, mothers with a diagnosis of anxiety (Manassis et al., 1994) or mood disorder in terms of major depression (Carter et al., 2001) or post-partum depression (Nonnenmacher et al., 2016; Esposito et al., 2017b) foster a disorganized attachment style. Early deprivation and economic poverty confer higher vulnerability to developmental disorders (Bizzego et al., 2020), even if the child is later exposed to an enriched environment (Luby et al., 2013; Mackes et al., 2020).

Both mothering and fathering behaviours provide unique caregiving practices in the parent-infant attachment within the family system (Brown et al., 2012). During pregnancy and in the early months of the baby, the role of the mother in meeting the physiological and care needs is prevalent worldwide. Some research suggest that during infancy, mothers tend to engage in emotional support and warmth, whereas fathers are involved in higher levels of active play (Fagan, 2020). More generally, low levels of overprotection and high levels of care typify the ideal parenting practices. High care is witnessed by warmth and affection of the parent sensitive to infants' requests, whereas low care implies neglect and application of maladaptive emotion regulation abilities. Low overprotection refers to parental ability to grant autonomy to the infant and increase his/her self-esteem (Silk et al., 2003). In contrast, high overprotection indicates that parents impose a manipulative psychological control over infant behaviour (e.g., hypercritical control, affect withdrawal, guilt induction, invalidation of feelings) (Barber, 1996; Morris et al., 2002; Neoh et al., 2021).

In the context of social interaction, humans can show a differential social competence concerning the quality of the social events they are experiencing or to the nature of the social distress stimuli to which they are exposed (Aron et al., 2005). An individual will exhibit a greater probability of prosocial behaviour if previously exposed to an early environment which boosted and appraised a range of social inclinations towards others (Sbarra and Hazan, 2008). By contrast, an individual will more likely perform a non-social behaviour if previously exposed to an uncommunicative and poorly stimulated early environment which restricted the amount of possible social conducts (Repetti et al., 2002), was not responsive to social cues or retreated from social experiences (Diamond et al., 2006). A more complex explanation can be described when genetic, physiological, and neuroendocrine systems (e.g., oxytocin, serotonin) are analysed in tune with psychological traits.

An exciting study by Dalsant et al. (2015) revealed that the quality of maternal bonding in childhood, assessed by the self-reported questionnaire Parental Bonding Instrument (Parker et al., 1979), alters the physiological responses to evolutionary salient distressing social stimuli (e.g., infant cry). Individuals who experienced a poor quality in their early parent-infant relationship, represented by low scores on both care and overprotection dimensions, reacted to the stressful condition with increased heart rate responses compared to individuals who reported a rich quality in the early parent-infant relationship, as indicated by high scores on both care and overprotection factors (Dalsant et al., 2015). Another research revealed that higher-quality maternal behaviour predicted a lower cortisol response as a better recovery from distress (Albers et al., 2008). These results illustrate that early parental bonding efficaciously predicts behavioural and physiological responses to conspecifics implicated in social interactions.

In summary, humans have an innate predisposition for social interaction starting from the nature of parental bonding and the quality in the early care of the parent-infant relationship. The so-called early environment represents a familiar habitat where the baby can experience significant relationships whose quality is associated with physical and mental health (Taylor et al., 2004). A large amount of research has explored how early life and distress have a longitudinal effect on human development (Cheung et al., 2002; Pechtel and Pizzagalli, 2011; Luby et al., 2017; Dunn et al., 2019).

1.3 Beyond the longitudinal effect of parent-child interactions: the influence of early and adult relationships on social development

Quality in mother-infant and father-infant interaction form a psychobiological signature on social development. A secure attachment modulates the social communication with the external inanimate and animate worlds in childhood (Fraley, 2002), even until adolescence - characterized by intensive social interaction with the peers and the partner (Fagot, 1997) - and adulthood (Rikhye et al., 2008) - characterised by the dimensional formation of the personality (Shaver and Brennan, 1992). The Prototype Hypothesis proposes that infant attachment representations persist during development and are carried into new relationships (Roisman et al., 2005; Madigan et al., 2015). Hence, parental bonding has significant long-term effects on social development and influences new relationships from infancy to adulthood. The characteristics of parental bonding in childhood even predict the quality of social relationships with peers and partners in adulthood (Feeney et al., 2007; Fraley et al., 2013). Beneficial early interaction with parents facilitates positive relationships with friends and reduces relations worries with the partner (e.g. less anxiety) decades later (Zayas et al., 2011). Conversely, maltreatment in toddlerhood are predictors of aggression, victimization ad depression in adulthood (Riggs and Kaminski, 2010). Individuals who reported an insecure attachment during infancy are inclined to develop an anxious resistant or avoidant adult attachment and are more likely to be affected by physical illness thirty years later (Puig et al., 2013). Similarly, anxious romantic attachment assessed by the Experience in Close Relationships-Revised at age 22 was predicted by an insecure attachment with parents and peers as measured by the Inventory of Parent and Peer Attachment at age 14 (Pascuzzo et al., 2013). A common explanation is that an insecure baby could become an insecure spouse, being concerned about the availability and capacity of the partner to take care of him/her. In unsecured individuals, anxiety activates the physiological system and maintains the attention on his/her figure when distressed. Anxiously-attached people may also apply inadequate support-seeking strategies such as controlling, clinging, or dependent-related behaviours (Nilsson et al., 2011).

Following the view of a continuous trajectory of development, Belsky et al. (2010) substantiated the developmental-evolutionary hypothesis that early attachment might program the timing of puberty in adolescence. Specifically, adolescents with an insecure infant attachment had an earlier start and end of puberty than those who were secure (Belsky et al., 2010). In support of the theory, dysfunctional relationships with caregivers seem to have long-term implications on neural development: McCormick et al. (2019) found that the dorsal striatum of affected adolescents was highly sensitive to rewards but barely sensitive to risk situations.

The aforementioned Evolutionary Theory of Socialization partly contrasts with the alternative Contextual Socialization Theory, which suggests that socialization takes place outside the family and is the result of intergroup processes rather than dyadic interactions (Harris, 1995). Even though the former is the most accredited, the latter has the merit to indicate that late relationships still have a social function and affect human development. Peer relationships in the group during adolescence and early adulthood represent a way to transmit culture and environmental modifications of society.

Being more and more immersed in society, adolescents observe and compare a range of social conducts and practices coming from groups, friends, and other parents or relatives than their own. Teenagers acquire various social competencies, representing context-specific social behaviour and personal expectations of others' behaviour. They can also recollect memories of their past relationship with their parents and their caregiving abilities.

Quality of peer and close relationships are also linked with physical and psychological outcomes (Mendle et al., 2007; Brunell et al., 2010; Simpson et al., 2011; Marion et al., 2013; Riggio et al., 2013). At a subcortical level, high interpersonal competencies are associated with higher white matter integrity of the major tracts of the right hemisphere (De Pisapia et al., 2014). A line of research interestingly claims that the main subcortical tracts of the right hemisphere - involved in social cognition, emotional perception, and nonverbal communication - are similarly activated during the first interpersonal relationship (e.g. with the mother) (Schore, 1997, 2000, 2001). The simple mentalization of the romantic partner seems to reduce the blood pressure reactivity during a stressful task (Bourassa et al., 2019). On the other hand, adults with insecure attachment representations exhibited a higher response of the hypothalamic-pituitary-adrenal (HPA) axis (increase in the adrenocorticotropic hormone - ACTH - and cortisol) and lower levels of oxytocin when compared to adults with secure attachment representations (Pierrehumbert et al., 2012). Before analysing the genetic correlates of social behaviour, cultural factors of social relationships are presented.

1.4 From micro to macro: culture belonging and social factors as determinants of social development

Social relationships can be very different between countries of the world. Cultural groups embody a set of beliefs and behaviours that benefit their members (Bornstein, 2012). Cultural and societal norms regulate socioemotional experiences at a macroscopic level (Mesquita and Frijda, 1992; Butler et al., 2007). In support of the Social Orientation Hypothesis, research suggests that cultures differ in the social orientation and cognitive habits of the inhabitants (Varnum et al., 2010). American, Western, and European societies are mainly characterised by an individualistic culture that endorses an independent social orientation focused on self-expression, self-governance, and cognitive analytic strategies (Nisbett et al., 2001). These societies are underpinned by personal well-being (e.g. beliefs, attitudes, needs) where the group promotes individual achievement (Markus and Kitayama, 1991). By contrast, Eastern and Asian societies show a collectivist culture that emphasises an interdependent social orientation focused on connection, harmony, self-criticism, and is based on holistic cognitive strategies (Kitayama et al., 2006). The group to which every individual adjusts the self is the core of these societies, regulated by social norms and group memberships (Heine, 2003).

At a microscopic level, ethnic origin and culture may influence parental cognitions and beliefs, which in turn affect the caregiving patterns towards the newborns (Rubin and Chung, 2013). The relationship between baby and caregiver, who operates as a psychobiological regulator Meaney (2001), can vary with the cultural membership. Parents from Western cultures hope that their children will gain total independence, assertiveness, optimism, confidence towards others and competence in the performances (Mesquita and Walker, 2003; Greenfield et al., 2003). Here, the act of making a personal choice allows the newborns to search for opportunities and affirm their identity (Tamis-LeMonda et al., 2008). The intrinsic motivation to learn is reinforced by families and schools, which hope for the expression of the maximum potential of the young generations (Harwood et al., 1999). Thus, high self-esteem and self-maximisation are the keys to promoting goals accomplishment in Western-oriented societies (Harwood et al., 1999; Miller et al., 2002). Simultaneously, parents from Eastern cultures prioritise interdependence, self-control, humility, and conformity to the group. Relational collectivism establishes a few prominent social institutions: family, groups, society. Closeness to relatives and partner(s) is the first value of Latino ("familism"), African, African-American ("extended kin") and South-East Asian ("family obligation") people who are united by a sense of allegiance, devotion and mutual assistance within the family (Gonzalez-Ramos et al., 1998; Keller et al., 2006; Tamis-LeMonda et al., 2008). Being a member of a group, toddlers learn to think about the consequences on others before acting. The single individual contributes to the emergence of society and favours social harmony (the Latino American "simpatia") (Triandis et al., 1984). Education here prioritises respect (the Latin American "respeto") to people belonging to different levels of the vertical hierarchy and obedience to authority (rule-following) (Chao et al., 2002).

In sum, caregiving practices and emotional regulation strategies within and between cultures are largely expected (Friedlmeier et al., 2011; Halberstadt and Lozada, 2011). For instance, Italian, American, and Argentinian mothers showed comparable responses of love, indulgence and devotion to their children. Nevertheless, Italian mothers were more sensitive than those from USA and Argentina, and Italian children were more responsive than the others (Bornstein et al., 2008). Moreover, Raudino et al. (2013) assessed a group of English mothers and a group of Italian mothers through the Parent-Child Interaction Questionnaire (evaluation of maternal intrusiveness) and the Skills of Daily Living Checklist (evaluation of maternal autonomy granting). Results revealed that Italian mothers granted less autonomy to their children and displayed a higher level of overcontrol than English mothers.

Overall, the two poles of social and emotional competencies commonly explored in Western and Eastern-oriented societies, namely individualism and relatedness, can coexist in a dynamic context and be expressed to a certain degree. For example, Hong Kong mothers, mostly educated by a Western system, endorse both (Chan et al., 2009). Cultural exceptions should also be acknowledged. Compared to American and Thai people Neff et al. (2008) observed that Taiwanese individuals had lower levels of self-compassion, a typical Asian construct of tolerance and resilience.

Experts define power or interpersonal distance as the construct which rationalises the relationship between family and culture (Triandis and

Gelfand, 1998; Hofstede, 2001). Egalitarian parents typically from Western-oriented horizontal societies engage in dialectical and turn-taking strategies which induce the child to lead the play or the conversation. An example comes from German caregivers who reinforce mutual face-to-face interactions, as opposed to the power-distant strategies of the Cameroonian Nso (Keller et al., 2005). As in this last case, but also in most Asian and African countries, power-distant parents adopt top-down conversational strategies and discourage direct or equal approaches not accepted in a vertical society (Keller et al., 2005).

At a behavioural level, Western caregiving makes the parental warmth through physical or verbal expressions of affection (e.g., kissing, hugging, caressing, praising) explicit (Wu and Chao, 2011). Eastern caregiving conversely tends towards less likely externalisation of love and instead favours close supervision, educational support and commitment (Deater-Deckard et al., 2011). Accounting for the cultural differences, parents respond differently to their children's failures and successes. Given that Eastern cultures believe that self-improvement is a part of the growth path, Asian parents minimise success and underline failure (Miller et al., 1997; Ng et al., 2007). Western cultures consider the outcome of the performance as strategic, thus persuading parents to promote qualities that increase the probability of success over failures to their children (Miller et al., 1997; Heine, 2003). In a study, American students reported that their mothers downplayed the academic failure and emphasised the academic success, while Chinese students reported the opposite behaviour from their mothers (Ng et al., 2007). In the same way, American mothers were found to laud their toddlers to increase their self-esteem, whereas Taiwanese mothers assumed self-esteem counterproductive to children's ability to learn from corrections (Miller et al., 2002). In recent research Neoh et al. (2021) found that parental bonding affects the perception of criticism differently between the United States, Italy, and Singapore, proving that parenting has a major effect on emotional regulation worldwide with cultural differences. Specifically, higher levels of parental overprotection were likely to increase the tendency to perceive criticism as destructive. This was true especially for USA participants when compared to Italians and Singaporeans.

In the context of socialisation, the same behavioural (accuracy) and neurophysiological (arousal and frontal asymmetry) indexes of facial recognition may be affected by the ethnic origin of the observed faces (Bonassi et al., 2021e). American and European children perform better in emotional recognition than Japanese children (Matsumoto and Kishimoto, 1983) and better in emotional expression (Wang, 2003; Li, 2006). To enhance the emotional regulation (Friedlmeier et al., 2011), Euro-American parents tend to encourage children's expression and avoid minimisation or punishment (Wong et al., 2009). Chinese and Indian parents believe that minimisation of caregiving responses is relevant as expressive encouragement (Vidhatri Raval and Martini, 2009; Tao et al., 2010). Nonetheless, Vidhatri Raval and Martini (2009) noted that mothers from middle classes more likely accepted the expression of negative emotions - as Western-oriented people did - than mothers from non-educated and disadvantaged urban classes. Chan et al. (2009) identified alternative strategies like - talking about causes and effects of emotions (response training) - or - reflecting on the moral reasons of emotions (reflection-enhancing).

Like other behaviours, response training resulted from a standard parental behaviour across Western and Eastern cultures (Wang, 2006). Although caregiving practices can be mostly culture-specific (e.g., beliefs on child development, competencies in caregiving, ages for developmental stages, when and how to care), parental cognition may be cross-cultural (Bornstein, 2012). Firstly, all the parents in the world wish the best for their children in terms of physical health, psychological well-being, social tuning, educational achievement, and economic security (Bornstein, 2012). Secondly, the mechanisms underlying the parent-infant relationship are shared. As explained in the second paragraph, the Theory of Attachment postulates that developing internal working models in the first years will shape lifelong social interactions, independently from cultural belonging. Likewise, the Social Learning Theory assumes that newborns could learn by imitation or modelling, thus simply observing and watching others worldwide (Bandura and Walters, 1977; Bornstein, 2012). However, environment and culture alone cannot explain the attachment or social behaviour variance.

1.5 Early programming: genetic basis of social behaviour

Human traits are genetically encoded. Any human characteristic (phenotype) originates from the genetic code (genotype), representing the foundation of life. In the form of a double helix[1]), the DNA (deoxyribonucleic acid) carries the instructions of human development. It programs the biological mechanisms of expression, transport and recovery of proteins, neurotransmitters, and hormones in response to life events. In the last three decades, researchers understood that social behaviour could have biological correlates and be genetically founded (Ebstein et al., 2010). Therefore, developmental psychobiology has investigated how genes modulated behaviour and physiology in response to social distress and social cues. Genes, behaviour and brain are bridged by dynamic molecular pathways through which genetic variations predispose brain functions to social behaviour and, vice versa, social information from the environment adjusts gene expression in the brain to affect behaviour (Robinson et al., 2008).

Different methodological tools have been adopted to establish phenotypes' genetic basis. Twin studies (dizygotic versus monozygotic[2]) have contributed to understanding the effect of shared and non-shared environment on the phenotype (Plomin et al., 2003; Caspers et al., 2007). A

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[1] The double strands are composed of nucleotides, linear sequences of sugar called deoxyribose, a phosphate group and one of four nitrogenous nucleobases adenine (A), cytosine (C), thymine (T) or guanine (G).

[2] Monozygotic twins share all of the genetic sequence; dizygotic twins share 50% of the genetic code.

second opportunity is offered by the Candidate Gene Studies (CGS) in which one or more Single Nucleotide Polymorphisms[3] (SNPs) were selected a-priori when involved in the biological mechanisms of the target phenotype[4] (Bonassi et al., 2017). Another alternative in neurogenetics can be the Genome-Wide Association Studies (GWAS) that compare multiple SNP frequencies (from hundreds to more than a million) across quantitative phenotypes to find the genetic region that partly or mostly explain the phenotypic variance (Brookes et al., 2006).

Most of the scientific production in the field has focused on few meaningful genes, each related to hormones or neurotransmitters involved in the social and affective brain (Raby et al., 2012): the Oxytocin Receptor Gene (*OXTR*) (MacDonald and MacDonald, 2010), the Arginine Vasopressin Receptor Gene (AVPR) (Pearce et al., 2017), the Serotonin Transporter Gene (5-HTTLPR) (Homberg and Lesch, 2011), the catechol-O-methyltransferase gene (COMT) (Van IJzendoorn et al., 2008) and the Dopamine Receptor Gene (DRD4) (Van Ijzendoorn and Bakermans-Kranenburg, 2006). Here, the attention is focused on *OXTR* and 5-HTTLPR to introduce the studies that are the focus of the present dissertation (see Chapters 2,3,4).

The *OXTR*[5] is a protein-coding gene that acts as an oxytocin receptor (OT). OT gene expression oversees the magnocellular neurons of the supraoptic and paraventricular nuclei of the hypothalamus (Gimpl and Fahrenholz, 2001). OT is an abundant nonapeptide known as the “love hormone”, as it is produced with high levels during the falling-in-love stage, affective behaviours (e.g., hugging, kissing) (Light et al., 2005) sexual activity (e.g., erection, orgasm). OT is also implicated in physiological functions such as parturition (e.g., increasing the contractions

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[3] A Single Nucleotide Polymorphism is a genetic region characterized by a variation in one nitrogenous base of two possible forms called alleles. An allele is an alternative variation of a given gene due to chromosomal alterations or gene mutations that alter the target gene’s protein encoded.

[4] This methodology is embodied in the studies presented in the following chapters

[5] *OXTR* contains three introns and four exons, which encodes aminoacids. Dozens of SNPs have been recognized within the *OXTR*.

of the muscles in utero) and breastfeeding. Therefore, OT is released by the pituitary gland in the circulation system to aid reproductive, social, and emotional functions (Kirsch et al., 2005; Costa et al., 2009; Skuse and Gallagher, 2011). In the context of human relationships, the oxytocinergic system is highly related to trust, empathy, prosocial behaviour (Kosfeld et al., 2005; Kumsta and Heinrichs, 2013), and favours cooperation against the competition in intergroup conflicts (De Dreu et al., 2010).

Intranasal dosage of OT was found to increase the self-perception of personality in individuals who tended to overrate their openness to experiences and values, warmth, and altruism after the dosage (Cardoso et al., 2012). OT may even promote an oversensitivity to emotion: participants with an intranasal administration of OT rated emotions in facial stimuli as expressing greater intensity than those receiving a placebo (Cardoso et al., 2014). However, OT could not have only positive effects as reported by Bartz et al. (2010): when the OT was assumed, adults who had a secure maternal attachment recollected their mothers as more caring compared to the control group (e.g., ones under placebo effect), whereas adults who had an anxious maternal attachment recollected their mothers as less caring than the controls. As demonstrated, the oxytocinergic system is combined with the dopamine reward system (Love, 2014). The Social Salience Hypothesis suggests that direct projections of the oxytocinergic system may boost the release of dopamine neurons in the ventral tegmental area (VTA) to enhance the salience to social cues[6] (Shamay-Tsoory and Abu-Akel, 2016; Peled-Avron et al., 2020). For instance, OT may enhance not only the attractiveness of the partner but also the selective neural response towards the partner, proving that this mechanism is pair-bonding specific (Scheele et al., 2013).

Allele variations in an SNP (AG/AA versus GG) of the *OXTR* (e.g., rs53576) could also confer different dispositional empathy and stress re-

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[6] Salient stimuli are alerting and are therefore processed by VTA, amygdala, and nucleus accumbens whose response evaluate their valence through compensatory dopaminergic-oxytocinergic mechanisms.

activity (Rodrigues et al., 2009; Chen et al., 2011a). Several polymorphisms of the *OXTR* (rs53576, rs2254298, rs2228485) are associated with positive and negative affect as well as emotional loneliness (Lucht et al., 2009). A deficit in the functional activation of the amygdala and altered hypothalamic structures in processing social cues have been observed in humans carrying an *OXTR* risk allele (rs53576 A/A) (Tost et al., 2010). In the context of atypical social functioning, a haplotype[7] (e.g., rs2254298 and rs53576) was linked to repetitive behaviours, cognitive deficits, and alterations of the brain structure attributable to autism (Wu et al., 2005; Wermter et al., 2010) and other developmental disorders (Carollo et al., 2021b).

The oxytocinergic system also interacts with the serotoninergic system in the regulation of reproduction, caregiving, socialization and emotions (Lefevre et al., 2017; Cataldo et al., 2018b). OT and serotonin (5-HT) neurons overlap in the hypothalamic nuclei, thus regulating their release of neurotransmitters to each other (Mottolese et al., 2014). Both these neuromodulators control the approach-avoidance behaviour: OT supports closeness and proximity for affiliative needs, while 5-HT promotes defensive and aversive dispositions for evolutionary reasons (Mottolese et al., 2014; Gellner et al., 2021). Serotonin transmission also influences cognition and motor activity and is responsible for mood (e.g., major depression), anxiety, and personality disorders (Pourhamzeh et al., 2021). Lower levels of 5-HT directly influence decision making, induce fairness and reduce impulsivity (Crockett et al., 2008). A decrease in the serotonin receptors (e.g., 5-HT1A) during development has long-lasting implications, such as lower social attitudes and higher anxiety (Donaldson et al., 2014). The gene SLC6A4 encodes the transporter, moving 5-HT from the synaptic cleft to the pre-synaptic neuron. *5-HTTLPR* represents the SLC6A4-linked polymorphic region and can show different versions of its alleles: short or long. The short allele produces fewer 5-HT transporters and proteins than the long allele, thus increasing the

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[7] A haplotype refers to a combination of alleles or a set of SNPS.

concentration of 5-HT in the synaptic cleft (Canli and Lesch, 2007). The short variations are therefore associated with risk factors for major psychiatric disorders. The parental short variant of the 5-HTTLPR predicts negative parenting behaviour, lower sensitivity and higher child distress (Cents et al., 2014; Morgan et al., 2018). However, a longitudinal investigation on the genetic effects of *OXTR*, DRD4, and 5-HTTLPR found that attachment security from infancy to adulthood and romantic bonding was only moderated by the OT circuit (Lee Raby et al., 2013b).

In conclusion, environmental, cultural and genetic factors and individual characteristics can shape social traits. However, multiple mechanisms can explain such factors' integration and simultaneous effects on social development.

1.6 Gene-Environment and Gene-Culture interaction models of development

A set of genes identifies a pool of potential metabolic, neural, physiological, or behavioural manifestations. When the individual genotype directly affects the phenotype, a genetic predisposition is a preponderant and sufficient condition to develop a disease in humans. Take the case of early blindness (Riazuddin et al., 2010) or deafness (Parker and Bitner-Glindzicz, 2015) or congenital amusia (Peretz, 2016): genes constrain the expression of the phenotype (e.g., visual deprivation), which, in turn, narrow the environmental stimulation (e.g., visual impairment). Because of mutations in the genes, eyesight recovery will be not plausible, but blindness will not be exempt from developmental plasticity due to compensatory strategies (Collignon et al., 2006), sensory substitutions (Striem-Amit et al., 2012) or an enriching environment (Bryck and Fisher, 2012). Supporting the Neural Darwinism Theory, the functionality of a lacking sensory modality (e.g., visual ability) will be maintained in the related neural structures by the afferent inputs from brain areas that encode other sensory modalities (e.g., acoustic, tactile, or olfactory information) (Edelman, 1993; Renier et al., 2014). This process is also known as cross-modal plasticity phenomena and illustrates how environment and experience affect gene expression (Bavelier and Neville, 2002). Although genes define the traits of a phenotype a-priori, such traits can be expressed only when specific environmental conditions are met. In other words, the environment represents a pool of resources that can advantage or disadvantage the expression of the phenotype. For instance, the Innateness Hypothesis predicts that language is innate with a clear biological basis; thus, this allows a child to develop grammar spontaneously (Nowak and Komarova, 2001). However, a child subject to social impoverishment and linguistic deprivation will not be able to hear some sentences proper to learn grammar (Onnis et al., 2018). A similar environment is poor in stimuli and does not enable the development of the trait (e.g., high verbal skills) or the function (e.g., linguistic ability), even though it is genetically founded. For this reason, the Ecological Systems Theory by Bronfenbrenner (1977) has the merit to underline the necessity of environmental conditions (internal and external) supporting the genetic programming. In this view, human traits are the result of bidirectional interactions between the genetic components and the complex environment (e.g., formed by microsystems and macrosystems) across time (Tudge et al., 2009).

Based on these examples, three concurrent mechanisms can be summarized: a) genes predispose the phenotype, outline the possible experiences, and influence the exposure to the environment (G); b) environment affects gene expression (e.g., as protective or risk factor), thus inducing remedial effects on the development of the phenotype (E); c) genetic predispositions and environmental factors interact and moderate each other (GxE). In the last decades, behavioural genetics has expanded the knowledge drastically on the interplay between genes and environment, proving that the social traits are partially heritable and much influence accounts for shared (e.g., with family or peers) and non-shared environment (context-specific) (Silventoinen et al., 2020; Matthews and Turkheimer, 2021). Likewise, multiple genetic variants of the genome can be associated with a trait, and the weight of each variants' effect is combined into a polygenic score (Plomin, 2018). Polymorphisms, as well as polygenic scores and all the genetic associations, also vary across populations of different ancestries (Hyde et al., 2015; Martin et al., 2019). In molecular psychiatry, such investigations have contributed to the definition of the endophenotypes of a disorder which refer to measurable biological traits of a genetic substrate[8] (Gottesman and Gould, 2003).

More recently, epigenetics has inspected how environmental actions produce changes in the genetic expression with no alterations in the DNA sequence or structure (McGowan and Szyf, 2010). Even though epigenetic processes[9] share the same consequences of the genetic polymorphisms, they are potentially reversible as opposed to the genetic programming. Chromatic[10] modification and DNA methylation[11] are keys of the epigenetic machinery that can be remodelled by developmental variations or environmental risk factors (Moore et al., 2013). The same neurons can re-adjust their patterns of DNA methylation in response to physiological stress or environmental stimuli (Guo et al., 2011). Most of the variance of epigenetic mechanisms are explained by gene-by-environment interactions (Meaney, 2017; Matosin et al., 2018; Tops et al., 2019).

Scientific literature has established many gene-by-environment interactions with a direct and indirect effect on mammalian social behaviour (Belsky and Pluess, 2009b). As outlined in the previous paragraph, specific alleles of selected genes (e.g., *OXTR*) of the genome have been connected with pro-social and non-social behaviour. Many theoretical models have been proposed to explain social development in the inter-

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[8] An endophenotype bridges the genetic pathway with the behavioural phenotype and can be biochemical, endocrinological, neuroanatomical, neurophysiological, neuropsychological, or cognitive.

[9] Epigenome includes a series of chemical compounds and proteins that activates (DNA transcription) or silences the expression of a gene. Only accessible genes can be transcribed.

[10] Chromatin is contained in each eukaryote cell nucleus and is formed by a nucleosome and histones.

[11] Methylation involves the transfer of a methyl group onto the C5 position of the cytosine to form 5-methylcytosine (Moore et al., 2013).

dependence of genes and the environment. The Diathesis Stress Model suggests that some polymorphisms can be risk factors for the development of a trait (e.g., openness) or disorder (e.g., social anxiety disorder) when a hostile environment is present (Rende and Plomin, 1992). Here, a variant in the alleles' configuration of the helix predisposes a vulnerability (diathesis) that is elicited by stressful experiences (stress) (Jaffee et al., 2005). Individuals with a polygenic presence of risk alleles and exposed to stressors can develop a major depressive disorder (Colodro-Conde et al., 2018). For instance, children inclined to be anxious-avoidant and jointly excluded from peers are likely to show internalizing difficulties (Gazelle and Ladd, 2003). Conversely, other polymorphisms can be protective towards the harmful effects of adversity (Belsky and Pluess, 2013).

The Vantage Sensitivity Model mirrors the aforementioned and explains that some polymorphisms can be "promotive factors" for the development of a trait (e.g., empathy) or skill (e.g., communication) in the presence of a positive environment (Pluess and Belsky, 2013). Here, endogenous characteristics (genetic) advance a potential (vantage) that is prompted by favourable experiences (sensitivity). For instance, children homozygous for the T allele of the *OXTR* rs2268498 who attended a resilience-promoting intervention reported higher scores in life satisfaction than C-carriers (Pluess, 2015). With regards to 5-HTTLPR, anxiety symptoms of children homozygous for the short allele decreased more than symptoms of the children with the long allele (Eley et al., 2012). On the other hand, individuals genetically resistant to advantages do not benefit from promising conditions.

The Plasticity Genes Model offers an intertwined view of the two previous models. Within this theory, the mechanisms through which genes moderate individual sensitivity to environmental action are "plastic" and flexible (Bakermans-Kranenburg and Van IJzendoorn, 2007; Belsky et al., 2007; Belsky, 2013). Here, risk alleles enhance the sensitivity both to negative or positive influences, respectively inducing lower or higher responsivity (Boyce and Ellis, 2005). The core of the Differential-Susceptibility and Resilience Hypothesis proposes that humans carrying these alleles vary in their developmental plasticity regardless of the quality of conditions: such genotype is susceptible both to adaptive and maladaptive experiences or environments (Caspi et al., 2002, 2003). The protective alleles instead confer a resilience for any effect (Masten et al., 2021). Therefore, children with the sensitive genotype (e.g. 5-HTTLPR SS/SL) may develop high social skills and positive affect with a history of supportive parenting, whereas they may develop a high need for approval and negative affect with a history of neglect or maltreatment (Hankin et al., 2011; Caplan et al., 2019).

Overall, infants genetically sensitive to early adversities tend to lessen empathy levels, avoid others, and limit pro-social behaviours in social interaction, reinforcing the probability to develop a mental disorder (Poulin et al., 2012; Gong et al., 2017). In the clinical domain, experts have often described the Self Generated Environment Model (Esposito et al., 2017a): signals of atypically developed infants (e.g., Autism Spectrum Disorder with a genetic basis) which the parents do not correctly detect may impact the quality of caregiving and, thus, worsen the parent-infant relationship and the prognosis of the disorder (Lyons-Ruth, 2015).

All these models fit into the historical debate of nature ("genes determine behaviour") versus nurture ("environment and experiences determine behaviour") (Sameroff, 2010) and provide patterns of possible gene-by-environment mechanisms. Fewer pieces of research have tried to frame behavioural genetics into a broader scope of the investigation that could include cultural, societal, or geopolitical factors commonly under-investigated. Considering such a high number of variables can add further comprehensiveness (and complexity) to the understanding of social behaviour and attachment under an ecological perspective that binds genetics, environment (intended as the context of social relationships) and culture (or society) (Dato et al., 2017). Hence, mechanisms of gene-by-culture and gene-by-culture-by-environment interactions have been interestingly probed to depict a multi-domain representation of social behaviour (Chudek and Henrich, 2011; Gintis, 2011). For instance, some works have traced the gene-culture co-evolution to human sociality as a function of individualism and collectivism (Chiao and Blizinsky, 2010; Way and Lieberman, 2010). Genetic regions such as *OXTR* rs53576 are even sensitive to cultural norms in the regulation of socio-emotional behaviour (Kim et al., 2011a). To broaden the knowledge on the multifaceted nature of social behaviour, Chapter 2 presents a cross-cultural study on the longitudinal impact of gene-by-environment interactions in affecting the quality of romantic relationships (Cataldo et al., 2021a).

The studies considered up to this point focus on in-person social behaviour, such as attachment with parents, relationships with peers or partners, or a set of cognitive traits, functions or behaviour that are implicated in face-to-face social interactions. However, online sociability has raised a great deal of attention stimulating novel research across disciplines in the last years.

1.7 Beyond In-person social behaviour: the rise of online behaviour on Social Media application

With the advent of the second millennium, the opportunities emerging from the social environment has drastically changed the way humans relate to each other (O'Keeffe et al., 2011). Social relationships usually imply the existence of a couple or a group of people who are engaged in a social exchange, either verbal or gestural, and share the same space and time. People who are involved in face-to-face interactions (offline) can rely on spoken or body language and regulate their behaviour according to their speaking time and their proximity to others (for a review of theories and methods see (Hadley et al., 2022)). By contrast, social relationships in the virtual world (online) are more immediate and accessible: people become users of a social network and can communicate across space and time with fewer nonverbal cues and form new social ties with greater anonymity (Lieberman and Schroeder, 2020). Social media platforms offer novel opportunities to socialize with higher accessibility and control. Social messaging applications (e.g., WhatsApp, Viber, Telegram, Voxer, WeChat, Messenger, LINE, Hangout) have increased the frequency and positive valence of communication. That being said, depth and breadth are still exclusive to face-to-face interactions (Knop et al., 2016). Video-conference applications (e.g., Zoom, Webex, RingCentral, Go to Meeting, Google Meet, Microsoft Teams, Duo, Skype) have secured smart-work and distance learning through virtual meetings and digital lectures (Sevindik, 2010). Medical doctors and psychotherapists have firstly taken advantage of such instruments since the beginning of the recent COVID pandemics (Békés and Aafjes-van Doorn, 2020; Bashshur et al., 2020). Social networking sites (SNSs; e.g., Facebook, Instagram, Tik Tok, LinkedIn, Twitter, Reddit, Snapchat) support the rise of digital communities where users have the possibility to a) broadcast, publish (privately or publicly; momentary or permanently) and share contents (in different formats, e.g., posts, pictures, videos) or information (e.g., news, events, links, articles with different text length) in personal profiles (e.g., Facebook diary); b) receive comments or likes as a reward or approval of the spread content; c) observe and judge how other users appear, what they decide to show; d) provide feedback (e.g., comment, like or endorse) and compare users' behaviours (Haferkamp and Krämer, 2011; Meshi et al., 2015). The motivation that leads people to interact virtually seems to be universally shared (Joinson, 2008; Lee et al., 2015), although cross-cultural differences are instead found in the reward generated using the social networks. Reflecting a collectivist culture, Eastern populations dedicate virtual interaction to obtain social support from people, whereas Western populations tend to maximize the self-promotion to achieve a more positive standing, in line with an individualistic culture (Kim et al., 2011b; Sheldon et al., 2017).

Social media can elicit social behaviours that significantly converge or diverge from those elicited in face-to-face interactions (Buote et al., 2009). The Displacement Hypothesis proposes that more online social interactions would reveal less social support, increasing loneliness and self-efficacy (Nie, 2001; Nowland et al., 2018). This condition is usually observed in individuals with social deficits that recede into not satisfying virtual relationships. Here, the time spent online replaces offline opportunities for sociability, thus inducing more significant discomfort. For example, individuals diagnosed with Hikikomori syndrome are intensive users of the Internet and social media but withdraw from social experiences (Kato et al., 2019). By contrast, the Stimulation Hypothesis states that quality time in online social interactions would achieve high social support, decreasing loneliness and enhancing self-efficacy (Valkenburg and Peter, 2007; Nowland et al., 2018). An increasing number of posts on Facebook was indeed found to reduce the perceived solitude independently of the likes or comments provided by other users (Deters and Mehl, 2013). In this context, time spent online extends the social approaches implemented offline. Similarly, the Complementary Hypothesis argues that the higher the frequency of online interactions, the higher the quality in social relationships both online and offline, as well as fewer experiences of loneliness (MacDonald and Schermer, 2021). This hypothesis has the merit to underline that frequency can be related to the quality of social interactions and that online social interactions' performance echoes and even improves the quality of offline social interactions. This conception would adequately justify why family members and friends are the most contacted people by adolescents and adults both online and offline (Kanai et al., 2012; Subrahmanyam et al., 2008). The universal Social Brain Hypothesis asserts that the social group size (150 relationships at a time) is limited by cognitive constraints whose origins are evolutionary (e.g. in the brain volume and size) (Dunbar, 2012). A biological basis of the variation in social network size would propose that the number of friends in SNSs estimate the grey matter density in brain regions involved in social perception and associative memory, such as the entorhinal cortex, the superior temporal sulcus, and the left middle temporal gyrus (Kanai et al., 2012).

Human social cognition constrains online and offline social behaviours: online and offline interactions may be different instruments of the same cognitive faculty. Although online and offline social interactions follow divergent rules, they overlap when showing comparable human attitudes (e.g., people can be friendly online as well as offline), cognitive biases (e.g., people can believe in misinformation both online and offline) and neural functioning (e.g., the social brain is activated when online or offline socialization occur) (Cinelli et al., 2021). From a neuroscientific standpoint, researchers mapped different brain regions associated with (and not just) online social behaviours (Meshi et al., 2015). The propagation and the reception of social messages (either online or offline) are associated with the activation of the dorsomedial prefrontal cortex, the temporal-parietal junction, and the precuneus (Falk et al., 2012; Schilbach, 2014). The publication of posts about themselves activates self-referential thinking, which positively correlates with the higher metabolic activity of the medial prefrontal cortex (Northoff et al., 2006; Tamir and Mitchell, 2012). Any form of approval and recognition as positive rewards (e.g., a like or a friend request) elicit the response of the ventromedial prefrontal cortex, the ventral striatum, and the ventral tegmental area (Fareri and Delgado, 2014; Korn et al., 2012).

Overall, associations between online social behaviour and psychological resilience versus vulnerability could depend on several elements, such as duration, frequency, and purpose of SNS usage and technological devices (e.g., smartphone, tablet, computer) (MacDonald and Schermer, 2021). On the one hand, online social interactions on the Internet stimulate many cognitive functions such as attentional capacities for the visual stimuli selection, memory processing for the storage of a large amount of information, and social cognition for the ability to identify with other users (Firth et al., 2019). Digital competencies mature in early infancy and enable toddlers to know an alternative communication system through devices. For example, infants gain proper knowledge of touchscreen properties by 15 months (Ziemer et al., 2021). Augmentative technology can assist children with disabilities to reach their developmental goals within an enriching environment (Judge et al., 2010; Pasqualotto et al., 2022). Parents introduce their kids to online games, streaming movies and internet applications (Shields and Behrman, 2000; Vandewater et al., 2007). The frequency of parental use of mobile media predicts how children use mobile media, suggesting an inter-generational transmission of digital know-how (Levine et al., 2019). Higher education purposes also inspire parents to participate in their children's media activities (Levine et al., 2019). On the path paved by parents, schools teach the benefits and the risks associated with the use of technologies and social media (Baker et al., 2009). With the advent of adolescence, teenagers acquire increasing autonomy in web browsing, form new online contacts, and turn out to be highly sensitive to emotion-arousing media (Crone and Konijn, 2018).

Conversely, high frequency of SNSs use, especially Facebook and Instagram is associated with depressive symptoms (Rosenquist et al., 2011; Lin et al., 2016), low self-esteem (Valkenburg et al., 2006), life (Kross et al., 2013) and body dissatisfaction (Sherlock and Wagstaff, 2018). Curiously, the time spent on the SNSs is negatively associated with the grades' average of college students (Junco, 2012b). At a clinical level, a diagnosis of major depression can accurately predict the increase of Instagram posting in time (Frison and Eggermont, 2017). Anxious users tend to spend much time on Facebook, probably seeking acceptance from others and limiting criticism on their content (McCord et al., 2014). Notably, a high need for self-presentation is a mediator that regulates the positive association between attachment anxiety and SNS addiction and the negative association between attachment avoidance and SNS addiction (Chen, 2019).

During development, the quality in the relationship with parents and peers can also be a protective or risk factor also in the online environment (DâĂŹArienzo et al., 2019). Infant and adult attachments moderate attention-seeking media behaviour and are related to the sensitivity to social feedback in SNSs (Lee, 2013; Flynn et al., 2018). A preliminary study (Gobbi et al., 2020) found that the relationship between the levels of maternal care and the number of friends on Facebook is linear with solid evidence. Facebook withdrawal, conflict, and relapse are negatively linked with higher levels of trust towards parents, but are positively linked with higher levels of alienation towards peers (Badenes-Ribera et al., 2019). Likewise, a psycho-pathological risk for Instagram addiction is traced back to a worse attachment bond with parents and peers (Ballarotto et al., 2021). Conversely, higher promotion of the body in the form of Instagram posts lead to Instagram-related conflict in the couple and undermine the romantic relationship (Ridgway and Clayton, 2016). Overall, adults who reported low levels of extraversion and openness (avoidant attachment) show a reduced SNS activity (Hart et al., 2015), while those who reported negative emotions and high worry on other users' judgment (anxious attachment) display an intensive SNS activity (Oldmeadow et al., 2013). Surprisingly, (Konok et al., 2016) observed that adults who were separated from their mobile (mobile attachment) exhibited comparable responses to those performed by infants separated from their mothers (infant attachment), such as proximity seeking behaviours and physiological distress (Konok et al., 2017).

Social cognition, attachment dimensions, and personality traits have a significant impact on the social sensitivity to social media (Correa et al., 2010; Jenkins-Guarnieri et al., 2013). When the Big Five main personality dimensions are considered (McCrae and Costa Jr, 1999; Costa Jr and McCrae, 1992), the time spent on the SNS and the frequency of SNS usage are positively predicted by extraversion, agreeableness, and conscientiousness, but negatively predicted by openness and neuroticism Skues et al. (2012); Brailovskaia and Margraf (2016). On the contrary, personality traits are predicted by SNS features (e.g., Facebook posts, Instagram pictures, Twitter texts) (Ferwerda et al., 2015). Among several personality disorders, the narcissistic personality correlates with the social network addiction disorder (Andreassen et al., 2017). More generally, problematic usages of the Internet are pervasive worldwide and incorporate a range of Internet-related disorders which are characterized by impairment in different life spheres, such as excessive and compulsive gaming, porn video seeking, buying, gambling, streaming, or using SNSs (Fineberg et al., 2018; Moor and Anderson, 2019; Cataldo et al., 2021b). Individual and psychosocial differences of online and offline social behaviours have been discussed. Given that all human behaviours are phylogenetically determined by biological factors and ontogenetically modelled by environmental patterns, it is likely that online (as well offline) social attitudes could result from the synergies of culture, genes and environment. To test this hypothesis and cover this gap in the literature, Chapter 3 and 4 report two studies that probe potential gene-by-environment interactions as determinants of Instagram social behaviour (Bonassi et al., 2020b; Carollo et al., 2021a).

Chapter 2

How does early caregiving interact with cultural and genetic factors in moderating adult attachment and in-person social attitudes?

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[0] Chapter based on a preregistered and published study:

Study 1. Cataldo, I., Bonassi, A., Lepri, B., Foo, J. N., Setoh, P., Esposito, G. (2021). Recalled parental bonding interacts with oxytocin receptor gene polymorphism in modulating anxiety and avoidance in adult relationships. *Brain sciences*, 11(4), 496. DOI: 10.3390/brainsci11040496.

The research presented in this chapter is linked to the following published studies of the research project:

Study A. Bonassi A., Cataldo I., Gabrieli G., Lepri B., Esposito G. (2021). Serotonin Transporter Gene Polymorphisms and Maternal Overprotection Regulate Adult Social Expectations on Close Relationships. *Brain sciences* 11(4), 496. DOI: 10.3390/brainsci11091123.

Study B. Bonassi A., Cataldo I., Tandiono M., Foo J.N., Lepri B., Esposito G. (2021). Effect of early paternal caregiving and genotype rs25531 polymorphisms on the adult relationship with the partner. *European Neuropsychopharmacology* 44(6), S9-S10. DOI: 10.1016/j.euroneuro.2021.01.019.

Study C. Bonassi, A., Cataldo, I., Tandiono, M., Foo, J. N., Lepri, B., Esposito, G. (2021). Genotype rs25531 polymorphisms and quality in peer relationships adjust the neural response of the anterior prefrontal cortex to cry. European Neuropsychopharmacology, 53, S380-S381. DOI: 10.1016/j.euroneuro.2021.10.488.

2.1 Introduction

As described in Chapter 1, fundamental works in disciplines related to developmental psychology have demonstrated that early social interactions with caregivers influence different aspects of child development, such as social relationships (Bowlby, 1973; Parker et al., 1979; Zafiropoulou et al., 2014), academic performance (Shin et al., 2012), response to stress (Francis and Meaney, 1999; Hane et al., 2008), individual well-being, and risk for psychopathology (Picardi et al., 2013; Rogosch et al., 1995; Shaver and Mikulincer, 2002; Reti et al., 2002). In addition, emotion-related skills in children like interpretation, regulation, and communication are built on the emotional and social relationships they share with their close ones (Spinrad and Gal, 2018). Therefore, it is likely that positive parenting practices, like higher levels of warmth, care, and sensitivity, will result in more adaptive emotion-regulation skills (Morris et al., 2007). The quality of parental bonding influences the development of top-down processes of emotional regulation, which could potentially shape social interactions and physiological responses in individuals. The ability to perceive typical social situations as non-threatening and risk-free also has implications for the autonomic nervous system (Porges, 2003). According to the literature, ideal parental practices can be described in terms of higher levels of care and lower overprotection. In fact, care allows individuals to be less restrained in social interactions, while overprotection diminishes the effectiveness of emotional regulation and the attitude about exploring new social situations. As a consequence, less positive caregiving patterns are also relevant to the manifestation of anxiety in social relationships (Rork and Morris, 2009).

According to the original theories on attachment by Bowlby and Ainsworth, attachment-specific features were considered to extend beyond cultural boundaries or parenting practices; in other words, Bowlby's and Ainsworth's original theory was considered to be culturally universal in the sense that parental behavior that is sensitive to the child's needs will result in attachment security across a diverse array of cultural and ecological contexts. Despite this assumption, the ecological components of attachment have always been seen as an important factor that needs to be taken into account, together with other features that might play a role in child-rearing behavior, such as socioeconomic status or ethnicity. In fact, one of the major concerns in the attachment-related research fields is the limitation due to results coming primarily from countries belonging to Western societies. With regards to cultural studies, Ainsworth's canonical work in Uganda and Baltimore underlined that processes related to maternal behavior reflect specific universal features that cross cultural, geographic, and linguistic boundaries (Ainsworth, 1967). In their research based on a sample of Japanese mothers, Behrens et al. (2007) found that maternal attachment was predictive of the child's attachment classification with a distribution comparable to global results. In a review on parental sensitivity in ethnic minority families, Mesman et al. (2012) highlighted the positive role of a secure pattern of attachment on children's development. Central to the quality of parenting practices and attachment are the dimensions of care and protection, encompassed in the construct of parental bonding (Parker et al., 1979). Parental care refers to the sensitivity of parents towards the child's needs (emotional, physical, psychological), while parental overprotection refers to the excessive restrictions (emotional, physical, psychological) imposed on the child. Partially inconsistent results have been described in a recent work on the link between the caregiver's warmth and levels of anxiety and avoidance in adult attachment in a Chinese population (Sun et al., 2010).

2.1.1 Familial Bonds in Italy and Singapore

In light of these considerations, it appears clear that, to have a proper understanding of parental bonds, it is essential to take a wider look at the concept of the familial nucleus according to the country where these family units are immersed. In the current study, we focused on two countries, one more Western oriented (Italy) and another one representative of a non-Western model (Singapore). In Italy, which is configured within individualistic countries, family is seen as an expanded network of relationships and ties, where much attention is given to the child. The relationship that forms between parent and child tends to be supportive and encouraging towards independence, presenting high levels of emotional bonding (Laudani et al., 2014). On the other hand, Singapore is described as a multicultural context, comprised of a majority of Chinese, Indian, and Malay families. In Singapore, which belongs to a collectivist culture, family is considered the first group a person joins in his/her life. The family frame belongs to a collectivist scaffolding, like other Asian countries, where interdependent relationships occur on a social and familiar level, especially for Chinese and Indian households. However, for all ethnicities, the extended family traditionally used to live with the original family, and parental control over the children was extended until adulthood. With the sudden rise of technology and globalization, it is difficult, for the Singaporeans, to maintain a multigenerational structure in families, and many people decide either to live alone or not to have children. Furthermore, parental roles change for those who decide to have babies, especially in the last couple of decades: if the hierarchy once used to be based on a patriarchal model, with the father having disciplinary power and the mother staying at home taking care of family duties, now both parents share the care of their children. Although evidence coming from different cultures and ethnicities has been reported and discussed, concerns about the application of Western-based methodologies to non-Western environments still remain. In fact, attachment-related mechanisms are, in turn, influenced by emotional communication, and the way emotions are expressed and experienced notably differs from country to country (Keller, 2018). Furthermore, while attachment dynamics have been profusely explored, little is known about the effect of processes that elapse between childhood and early adulthood, in the manifestation of dynamics in adult relationships.

2.1.2 *OXTR* rs53576

Considering the development of specific social characteristics as a result of the interaction between biological and environmental factors, it appears clear that behavioral facets might present a combination of genetic, environmental, and neurobiological factors. This involves the genetic regulation of neurotransmitters that are notably involved in the modulation of social functioning, such as the oxytocin receptor gene (*OXTR*) (Walum et al., 2012; Tost et al., 2010). Evidence in the literature reports results about the involvement of *OXTR* SNPs in modulating the response to social stressors (Feldman, 2012; Zink and Meyer-Lindenberg, 2012; Domes et al., 2007). Within the polymorphic region of *OXTR*, allelic variations of the single-nucleotide polymorphism rs53576 have been shown to be associated with different social behaviors. Specifically, the G allele appears to be linked with more optimal social development, which is described through higher levels of dispositional empathy (Rodrigues et al., 2009; Smith et al., 2014), favorable prosocial features (Truzzi et al., 2018; Senese et al., 2017; Rodrigues et al., 2009; Tost et al., 2010), and greater autonomic reactivity to social stressors (Norman et al., 2012). On the other hand, A/A homozygotes have shown overall poorer social traits (Thompson et al., 2011; Wu et al., 2012), reduced empathy accuracy Rodrigues et al. (2009), and positive affect (Lucht et al., 2009), all representing a less flexible social development. Although many results highlight the association between specific variations of the genotype and their determined social features, there are still some discrepancies in the literature (Apicella et al., 2010; Li et al., 2015; Bakermans-Kranenburg and van IJzendoorn, 2008). With specific regards to the interaction with perceived parental warmth, higher levels of paternal care have been found to be associated with an increased heart rate response towards social cues for individuals with a G/G variation in an Italian sample (Truzzi et al., 2018). A study by Kim and colleagues compared a Korean and an American population to investigate the interaction between perceived stress and

OXTR rs53576 variations in modulating the seeking of emotional support, suggesting that, among Americans, G-carriers were seeking more emotional social support compared to A/A homozygotes, while the same difference was not shown in the Korean sample. Moreover, they also compared Koreans raised in America and Koreans raised and living in Korea, finding greater emotional social support-seeking behavior in the first sample, hence highlighting the relevance of the cultural environment (Kim et al., 2010).

2.1.3 Current Study: Hypotheses

The wider purpose of the current study was to deepen our understanding of how the interaction between individual genetic features and the perception of parental warmth during childhood affects levels of anxiety and avoidance in adult relationships. The aim was to analyze the differences occurring in two different countries, like Italy and Singapore. The choice of these two contexts allowed a comparison of a Western country and a non-Western country, as environmental factors, such as the country one belongs to, may affect, on the one hand, the perception of parental features in childhood and, on the other hand, the formation of the behavioral constructs that drive social relationships. In order to explore parents' transmitted behavior towards the child (assessed in terms of warmth/care and overprotection), we used the Parental Bonding Instrument (PBI) by Parker et al. (1979). To measure the levels of anxiety and avoidance in adult relationships, we employed the revised version of the Experience in Close Relationships (ECR-R) (Fraley et al., 2000a). For the Singaporean sample, we used the original versions in English, while for the Italian sample, participants completed the translated and validated Italian versions (Scinto et al., 1999; Busonera et al., 2014a). We hence set two hypotheses on the Western (i.e., Italian) and Eastern (i.e., Singaporean) sample, respectively, and independently of the cultural differences.

HP1 *Gene*environment interaction on the Western sample*: We expected to find a statistically significant effect of the interaction between *OXTR* polymorphism and parental bonding features (assessed using the PBI scales) over the main features of adult social relationships (measured with the ECR-R), with Italian A-carriers showing different rates of distress in terms of anxiety and avoidance than G/G homozygotes when they reported low levels of parental care and high levels of parental overprotection;

HP2 *Gene*environment interaction on the Eastern sample*: We expected to observe a statistically significant effect of the interaction between *OXTR* polymorphism and parental bonding features (assessed using the PBI scales) over the main features of adult social relationships (measured with the ECR-R), with Singaporean G-carriers exhibiting different rates of distress in terms of anxiety and avoidance than A/A homozygotes when they recalled low levels of parental care and high levels of parental overprotection.

The predicted gene*environment interactions on the two separated samples could not however disclose a distinct pattern of adult attachment between Eastern and Western samples. Given the complexity of the multiple relationship between genetic factors, cultural influences, and early parental bonding on adult attachment, potential gene*culture interactions were finally hypothesized at an observational level:

HP3 *Culture*gene*environment interactions on the total sample:* We predicted a differential susceptibility of *OXTR* rs53576 to perceived parental bonding (assessed with the PBI subscales) between the Western (i.e., Italian) and the Eastern (i.e., Singaporean) groups in explaining the levels of anxiety and avoidance (measured using the ECR index.

2.2 Materials and Methods

The research was approved by the Ethical Committee of Nanyang Technological University (IRB-2015-08-020-01) and of the University of Trento

(Prot-2017-019). Informed consent was obtained from all participants, and the study was conducted following the Declaration of Helsinki. Participants were recruited through a social media platform (students' Facebook groups, for the Italian sample) and a web-based software research study participation and management system (Sona System, for the Singaporean sample) among non-parent students of the University of Trento, Italy, and Nanyang Technological University, Singapore. After informed consent was given, the online form of the questionnaires was sent through email to the participants (links to Qualtrics for the Singaporean sample and links to Google Modules for the Italian sample). Participants who gave consent for the genetic part of the experiment were contacted to set an appointment to obtain a buccal mucosa sample for genetic information. The genetic assessment was conducted on anonymized biosamples at the Nanyang Technological University (Singapore) and at the Department of Neurobiology and Behavior at Nagasaki University (Japan). Results from the questionnaires were anonymized at the beginning of the collection. The final group consisted of 313 participants that fully completed the two questionnaires and provided the experimenters with a DNA sample (Italian sample N = 97 (M = 38; F = 59); mean age = 23.01 (M = 23.58; F = 22.64), SD = 3.82 [range 18∼35]; Singaporean sample N = 216; M = 73; F = 143; mean age = 21.51, SD = 1.83 [range 18∼31]). The related dataset is available online on the Data Repository of the Nanyang Technological University (DR-NTU Data) (Esposito et al., 2021).

2.2.1 Questionnaires

Parental Bonding Instrument: The Parental Bonding Instrument (PBI) is a 50-item self-report questionnaire that investigates participants' perception of both maternal (25 items) and paternal (25 items) care and protection in their first 16 years of life. It was developed by Parker, Tupling, and Brown in 1979 using factor analysis from parents' self-reporting their childhood experiences, the results of which yielded two factors: warmth/care (hereafter referred to as care) and overprotection (Parker et al., 1979). The care scale (PBI_Care) measures the degree to which a mother or a father was empathetic and caring versus cold and indifferent. The overprotection scale (PBI_OverP) measures the extent to which a parent was intrusive or, conversely, fostered independence in the subject. The measure has been shown to have high reliability, stability over time, and no association with social desirability, neuroticism, or extroversion (Parker, 1989).

Experience in Close Relationships-Revised: In order to evaluate anxiety and avoidance levels in close relationships, the Experience in Close Relationships-Revised was employed (ECR-R; (Fraley et al., 2000a; Busonera et al., 2014a)). The 36-item self-report questionnaire assesses two major dimensions of an individual's attachment style (anxiety and avoidance) in a sentimental relationship. Both the anxiety and avoidance subscales consisted of 18 items each, rated on a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). The anxiety dimension measures insecurity, jealousy, and fear of abandonment as opposed to feeling secure about the availability and responsiveness of romantic partners. The avoidance dimension measures the feeling of discomfort being close to others and tendency to refrain from attachment. Instead of assigning participants to an attachment style category, this scale yields two separate dimension scores for each participant.

2.2.2 Genotyping

This study adopted the same DNA derivation and genotyping procedure used by Bonassi and colleagues (Bonassi et al., 2017), using ACGT, Inc. (Wheeling, IL). DNA was extracted from each kit using the Oragene DNA purifying reagent, then concentrations were assessed through spectroscopy (NanoDrop Technologies, USA). Concentrations for each sample were magnified through polymerase chain reaction (PCR) for the *OXTR* gene rs53576 region target. The forward and reverse primers that were used were 5-GCC CAC CAT GCT CTC CAC ATC-3 and 5-GCT GGA

CTC AGG AGG AAT AGG GAC-3.

For this DNA region, the frequency for the allelic distributions (A/A, A/G, G/G) differ among populations belonging to different ethnic groups. Although a unique consensus has still not been reached and may depend on the alleles' distributions within a specific sample, the A allele is usually combined with the same heterozygous group A/G in the Western samples, whereas the G allele is more commonly paired with the heterozygous group A/G in the Eastern samples (Wu et al., 2005; Apicella et al., 2010; Truzzi et al., 2018). In line with the existing literature, the present study followed the same paired allelic in the two different populations.

In cross-cultural investigations analyzing different ethnic groups as a whole, reducing the number of genetic groups, A/A is maintained in contrast with the combined couples A/G and G/G (Kim et al., 2010; Butovskaya et al., 2020). Here, Western participants (e.g., all Italian native participants with Caucasian ethnicity) having at least one A allele (A/A homozygotes or A/G) were classified into a single A-carriers group. Complementary to this, Eastern participants (e.g., all Singaporean native participants with Southeast-Asian ethnicity, namely 184 Chinese, 15 Malays, 8 Indian, 3 Caucasian, 3 Filipino, 1 Vietnamese, 1 Gurkha, and 1 Korean) having at least one G allele (G/G homozygotes or A/G) were treated as a single G-carriers group.

The averaged distribution of the different genotypes in the Caucasian population was 25–35% for A/A homozygotes and 65–75% for G-carriers[1], whereas the distribution in the Italian sample was 15% for A/A homozygotes and 85% for G-carriers. Specifically, genotype frequencies were as follows: A/A = 14 (14.43%), A/G = 35 (36.08%), G/G = 48 (49.49%). In the present Italian sample, the less frequent homozygous group A/A was merged with the heterozygous group A/G (A-carriers = 51%; G/G = 49%) before the analysis. Participants' age ($t = 1.761$, $p = 0.383$) and sex $X^2(1) = 0.016$, $p = 0.899$) did not significantly differ between

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[1] 1000 Genomes project

the G/G and A groups (see Table 2.1). As for the Singaporean sample, the allelic distribution in the East-Asian population was 65–75% for A/A homozygotes and 25–35% for G-carriers[2], whereas in our sample, the distributions were 37% for A/A homozygotes and 63% for G-carriers. Specifically, genotype frequencies were: A/A = 80 (37.04%), A/G = 94 (43.52%), and G/G = 42 (19.44%). Participants' age ($t = 0.481$, $p = 0.631$) and sex $X^2(1) = 0.189$, $p = 0.663$) did not significantly differ between the A/A and G groups (see Table 2.1).

	Age	
Sample	**Contrast between Genotypes**	***t***
Italian	G/G - A	1.76 (.38)
Singaporean	A/A - G	0.48 (.63)
	A/A - A/G	-0.81 (.88)
Total	A/A - G/G	0.42 (.41)
	G/G - A/G	-0.99 (.32)
	Sex	
Sample	**Contrast between Genotypes**	X^2***(1)***
Italian	G/G - A	0.02 (.90)
Singaporean	A/A - G	0.19 (.66)
Total	A/A - A/G - G/G	0.01 (.97)

Table 2.1: **Age**. Statistics of Student's *t*-test on age differences between rs53576 genetic groups within the Italian (G/G vs. A-carriers), Singaporean (A/A vs. G-carriers) and the Total sample (A/A vs. A/G; A/A vs. G/G; G/G vs. A/G). **Sex**. Statistics of Pearson's X^2 determine the difference between the frequency of males and females belonging to each genetic group for the Italian (G/G vs. A-carriers), Singaporean (A/A vs. G-carriers) and the Total sample (A/A vs. G/G vs. A/G). For each statistical test, the *p*-value is reported between parentheses.

Alleles' frequency distribution and Hardy–Weinberg equilibrium parameters are reported in Table 2.2. In the total sample, the distribution of the alleles was as follows: A/A = 94 (30.03%), A/G = 129 (41.21%), and G/G = 90 (28.75%). Since the genotype frequencies for the whole sample (total sample = Italian sample + Singaporean sample) did not satisfy the Hardy–Weinberg equilibrium, analyses focused on the three distinct allelic combinations within the frame of an exploratory approach. Participants' sex ($X^2(2) = 0.008$, $p = 0.996$) did not significantly differ between the three groups. Participants' age did not significantly differ between A/A and A/G ($t = -0.814$, $p = 0.883$), A/A and G/G ($t =$

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[2] 1000 Genomes project

0.417, $p = 0.413$), and G/G and A/G ($t = -0.991$, $p = 0.323$) (see Table 2.1).

Genotype	**A/A**	**A/G**	**G/G**	X^2	***p-value***
rs53576$_{\mathbf{ITA}}$	14 (14.43%)	35 (36.08%)	48 (49.49%)	3.05	.08
rs53576$_{\mathbf{SNG}}$	80 (37.04%)	94 (43.52%)	42 (19.44%)	2.24	.13
rs53576$_{\mathbf{Total}}$	94 (30.03%)	129 (41.21%)	90 (28-75%)	9.64	.002**

Table 2.2: Hardy-Weinberg Equilibrium results for *OXTR* rs53576 in the Italian sample, in the Singaporean sample, and in the total sample. The percentage frequency of each genetic group is reported between parentheses. **p<.01

2.2.3 Statistical Analyses

Data were analyzed with R (Version 4.0.0). Statistical tests were differently planned for hypothesis-driven and exploratory analysis. The hypothesis-driven tests were performed separately on the Italian and the Singaporean sample, whereas the exploratory tests were conducted on the total number of participants (total sample = Italian sample + Singaporean sample). Overall, the statistical analyses followed a common procedure of variables' evaluation and tests' application.

Preliminary Analyses

Before proceeding with the data analysis, we tested the internal validity of each questionnaire in both groups (Italy, Singapore). Preliminary tests were made in each population group to exclude any significant effect on the ECR-R-dependent variables that could be attributed to participants' sex and age for the exploratory analysis. Univariate and multivariate distributions of the PBI and ECR-R scores were inspected for normality and the presence of extreme values. Seventy-six observations (Italian sample = 27; Singaporean sample = 49) were found as having a value higher/lower than 2 *SDs* above/below the mean. Any artificial restriction (i.e., outliers' removal or treatment) was avoided to preserve the meaning associated with the scoring of each extreme observation. A high reliability of the subscales (see Table 2.3) also excluded potential biases due to extreme scores (Zijlstra et al., 2011).

Group	Subscale	Cronbach α	Skewness	Kurtosis	Mean (SD)	Median
Italy	Age	-	-	-	23.01 (3.82)	22
	PBI M_Care	0.93	-1.15*	0.71	26.33 (8.50)	28
	Squared PBI M_Care	-	-0.43	-0.88	764.70 (373.24)	784
	PBI M_OverP	0.78	0.72	0.18	16.40 (6.30)	16
	PBI F_Care	0.94	-0.49	-0.69	23.23 (9.30)	25
	PBI F_OverP	0.83	0.75	0.17	14.12 (7.01)	13
	ECR-R Anxiety	0.91	0.70	0.14	56.59 (20.10)	53
	ECR-R Avoidance	0.88	0.38	-0.39	35.12 (15.37)	33
Singapore	Age	-	-	-	21.51 (1.83)	21
	PBI M_Care	0.91	-0.66	-0.03	25.39 (6.99)	26
	PBI M_OverP	0.86	0.40	-0.01	15.09 (7.06)	15
	PBI F_Care	0.92	-0.28	-0.41	21.44 (8.14)	22
	PBI F_OverP	0.86	0.69	0.51	11.57 (6.63)	11
	ECR-R Anxiety	0.93	-0.04	-0.39	64.79 (20.61)	66.50
	ECR-R Avoidance	0.94	0.12	-0.51	40.31 (17.13)	40
Total	Age	-	-	-	21.97 (2.70)	22
	PBI M_Care	0.92	-0.86	0.36	25.68 (7.49)	27
	PBI M_OverP	0.83	0.45	0.09	15.50 (6.85)	15
	PBI F_Care	0.93	-0.32	-0.53	21.99 (8.54)	23
	PBI F_OverP	0.83	0.71	0.46	12.36 (6.84)	12
	ECR-R Anxiety	0.92	0.18	-0.44	62.28 (20.76)	62
	ECR-R Avoidance	0.92	0.22	-0.48	38.70 (16.75)	39

Table 2.3: Summary of Cronbach α, skewness and kurtosis for each subscale of the Parental Bonding Instrument and Experience in Close Relationships in the Italian sample, Singaporean sample and total sample. Statistics of age as continuous variable are also reported. * = squared transformation applied. M_Care and M_OverP refer to the maternal dimensions, whereas F_Care and F_OverP are related to the father.

Main Analyses

Exploratory correlation matrices were generated for the Italian, Singaporean, and total samples to probe possible associations among the continuous variables (e.g., PBI and ECR-R dimensions).

A series of hierarchical multiple regression (HMR) analyses was performed on the Italian and Singaporean sample separately to test the hypothesis that gene*environment interaction would predict the dependent variable (DV) adult anxiety (e.g., one series on the Italian sample, one series on the Singaporean sample). A series of HMR analyses was also conducted on the Italian and Singaporean sample separately to test the hypothesis that the gene*environment interaction would predict the DV adult avoidance (e.g., one series on the Italian sample, one series on the Singaporean sample). In summary, a six-step HMR was conducted for each ECR-R subscale (namely, anxiety and avoidance) as the DV in reference to each sample (see the models applied to each step in Table 2.4).

Italian Sample	
Step	**Tested Model**
1	ECR-Rvariable = *OXTR rs53576*
2	ECR-Rvariable = (*OXTR rs53576 + M_Care*)
3	ECR-Rvariable = (*OXTR rs53576 + M_Care + M_Overp*)
4	ECR-Rvariable = (*OXTR rs53576 + M_Care + M_Overp + F_Care*)
5	ECR-Rvariable = (*OXTR rs53576 + M_Care + M_Overp + F_Care + F_Overp*)
6	ECR-Rvariable = (*OXTR rs53576 * (M_Care + M_Overp + F_Care + F_Overp*)
Singaporean Sample	
Step	**Tested Model**
1	ECR-Rvariable = *OXTR rs53576*
2	ECR-Rvariable = (*OXTR rs53576 + M_Care*)
3	ECR-Rvariable = (*OXTR rs53576 + M_Care + M_Overp*)
4	ECR-Rvariable = (*OXTR rs53576 + M_Care + M_Overp + F_Care*)
5	ECR-Rvariable = (*OXTR rs53576 + M_Care + M_Overp + F_Care + F_Overp*)
6	ECR-Rvariable = (*OXTR rs53576 * (M_Care + M_Overp + F_Care + F_Overp*)
Total Sample	
Step	**Tested Model**
1	ECR-Rvariable = *Culture*
2	ECR-Rvariable = (*Culture + OXTR rs53576*)
3	ECR-Rvariable = (*Culture + OXTR rs53576 + M_Care*)
4	ECR-Rvariable = (*Culture + OXTR rs53576 + M_Care + M_Overp*)
5	ECR-Rvariable = (*Culture + OXTR rs53576 + M_Care + M_Overp + F_Care*)
6	ECR-Rvariable = (*Culture + OXTR rs53576 + M_Care + M_Overp + F_Care + F_Overp*)
7	ECR-Rvariable = (*Culture * OXTR rs53576 * (M_Care + M_Overp + F_Care + F_Overp*)

Table 2.4: As regards the Italian sample, for each ECR-R dimension (anxiety and avoidance separately) a six-steps hierarchical multiple regressions was performed with the *OXTR* gene genotype rs53576 as a between-subject factor (G/G and A-carriers) and the PBI dimensions (maternal mare, maternal overprotection, paternal care, paternal overprotection) as continuous predictors. As regards the Singaporean sample, for each ECR-R dimension (anxiety and avoidance individually) a six-steps hierarchical multiple regressions was performed with the *OXTR* gene genotype rs53576 as a between-subject factor (A/A and G-carriers) and the PBI dimensions (maternal mare, maternal overprotection, paternal care, paternal overprotection) as continuous predictors. As regards the total sample, for each ECR-R dimension (anxiety and avoidance distinctly) a seven-steps hierarchical multiple regressions was performed with the *OXTR* gene genotype rs53576 as a between-subject factor (A/A, A/G and G/G) and the PBI dimensions (maternal mare, maternal overprotection, paternal care, paternal overprotection) as continuous covariates.

Allelic variation for *OXTR* was entered at Stage 1 as a between-subjects factor of the regression to control for differences due to the genetics (Italian sample: G/G vs. A-carriers; Singaporean sample: A/A vs. G-carriers). Progressively, all the PBI subscales as continuous predictors were entered into each following step; specifically, maternal care was entered at Step 2, maternal overprotection at Step 3, paternal care at Step 4, and paternal overprotection at Step 5. In the final model (Step 6), the interaction between *OXTR* polymorphism variants and perceived parental bonding was tested.

A further series of HMR analyses was conducted on the total sample to test the exploratory hypothesis that culture would modulate the interaction between *OXTR* and early caregiving behavior on adult anxiety and avoidance as a unique DV (e.g., one series on the total sample for anxiety as the DV, one series on the total sample for avoidance as the DV). Therefore, in the total sample, an initial step was added in order to include the cultural variable (Italian vs. Singaporean) in the predictors of the regression model, for a total number of seven steps (see Table 2.4). Allelic groups for *OXTR* were here added at Stage 2 as a between-subjects factors (Total sample: A/A vs. A/G vs. G/G). Successively, all the PBI dimensions were singularly entered into each subsequent step following the order of administration of each sub-dimension of the PBI questionnaire. The final model (Step 7) was here defined by the interaction between culture, *OXTR* polymorphisms variants, and perceived parental bonding.

To compare the significance of each progressive model, the analysis of variance (ANOVA) was used to analyze the contribution of each predictor added at every step. As the contrast coding system for the categorical variables (e.g., culture and *OXTR* as factors) entered into the linear models, dummy coding was applied to compare each level of a given categorical variable to a fixed reference level. The factor *OXTR* presented two levels for the analysis on the Italian (reference level: A-carriers as 1; G/G as 2) and Singaporean (reference level: G/G as 1; A-carriers as 2) samples, but three levels were considered for the analysis on the total sample (reference level: A/A as 1; A/G as 2; G/G as 3). The factor culture included two levels for the analysis developed on the total sample (reference level: Singaporean as 1; Italian as 2).

Overall, the hierarchical regression allowed identifying the positive predictors of the dependent variable at different stages of increasing complexity. The final step was reached when all the variables defined by the hypotheses were included in the model. As described, the final models included the interaction between all the embedded variables (interactive model) as predicted by the hypotheses.

This type of regression is particularly targeted in research design with multiple variables (e.g., different contributing factors and/or continuous subscales), nested designs, and unpredictable outcomes or exploratory analyses (Bradley et al., 2001; Elgar et al., 2007) and was already applied in previous studies in this field (Kim et al., 2010; Kogan et al., 2011; Senese et al., 2017, 2019). Before conducting the HMR analyses, the related assumptions (multicollinearity, i.e., variance inflation factor, homogeneity of variance, i.e., Bartlett's test) were tested and satisfied. The post hoc statistical power was calculated for the final model of each series of HMR analysis of each sample using the G*Power software (Version 3.1) (Faul et al., 2009). The magnitude of each effect for the hierarchical linear models was estimated by R, R^2 and ΔR^2.

For each sample, the level of significance for the effects emerging from the final step of each HMR analysis was adjusted as a function of the two HMR analyses conducted on anxiety and avoidance, respectively (2 repeated measures for the Italian, Singaporean, and total sample separately; corrected $alpha = 0.025$). Bonferroni's method was chosen instead of alternative techniques to apply a more conservative correction.

For each sample, the significant main and interaction effects obtained from the final step of each series of HMR analysis were graphically represented by scatterplots with linear models and bar plots. A further assessment was advanced to inspect the direction of such effects. Pearson's r and Fisher's z tests evaluated the degree of association between the continuous independent variables and the dependent variables (Diedenhofen and Musch, 2015). Variables related to PBI subscales were also divided into two groups (low vs. high PBI dimension) using the median split procedure for post hoc tests. The median values used to divide the PBI variables into the "high" and "low" subgroups are reported in Table 2.3. Post hoc analyses were computed for significant results on ECR-R variables adopting Student's t-tests. Welch's t-tests were preferred over Student's t-tests when the variance of the comparing two groups from the normal population was different. A false discovery rate correction (e.g., Bonferroni's method) for the t-tests was considered to circumscribe the probability of committing a type I error. The magnitude of the significant effects for the *t*-test was estimated by Cohen's *d*.

With regard to the significant main effects, the mean differences of the given ECR-R variable between low and high PBI subscales ($\alpha = 0.05$) were tested (e.g., see below the main effects for the Italian, Singaporean, and total sample). Concerning the significant interactions between genotype and environment, low vs. high PBI levels were compared to analyze the differences between the genetic carriers on the ECR-R dimension (e.g., see below the effects for the Singaporean sample given the corrected $\alpha = 0.025$ and the total sample given the corrected $\alpha = 0.017$). In the context of the significant interactions between culture and environment, low vs. high PBI levels were contrasted to probe the differences between the Italian and Singaporean individuals (corrected $\alpha = 0.025$) on the ECR-R subscale (e.g., see below the effects for the total sample). In reference to the significant interactions between culture, genotype, and environment, low vs. high PBI levels were contrasted to inspect the differences between the genetic carriers from the Italian and Singaporean samples (corrected $\alpha = 0.025$) on the ECR-R variable (e.g., see below the effects for the total sample).

2.3 Results

2.3.1 Preliminary Results

The Cronbach's alpha coefficients ranged from 0.78 to 0.94, suggesting an overall very good internal consistency. In Table 2.3, all the Cronbach alpha values are listed, together with the main descriptive statistics of each sample. The psychometric features of the two instruments are compatible with those reported in a recent review on adult attachment assessment tools (Ravitz et al., 2010).

As observed in Table 2.3, acceptable skewness and kurtosis values, as well as visual inspection via density and quantile-quantile plots proved that the PBI and ECR-R subscales were normal univariate distributions (see

Table 2.3). Only the distribution of PBI maternal care skewed right in the Italian sample (skewness = 1.15; kurtosis = 0.17); thus, the variable was square-transformed (skewness = −0.43; kurtosis = −0.88) before analysis. The same approach was adopted by previous research in the field (Kim et al., 2010).

A differential Bonferroni correction was applied to each group in adjusting *alpha* (Italian sample: 4 repeated measures, corrected *alpha* = 0.0125; Singaporean sample: 4 repeated measures, corrected *alpha* = 0.0125; total sample: 6 repeated measures, corrected *alpha* = 0.008). No effects of sex nor age on the ECR-R dimensions were significant (see Table 2.5). However, a main effect of culture was observed on adult anxiety, whereas the effect of culture on adult avoidance did not survive the correction (see Table 2.5. This preliminary result confirmed the necessity to inspect the potential interaction between culture, genotype, and caregiving behavior, as hypothesized by *HP3*.

Sample	**ECR-R subscale**	**Variable**	***t* (df)**	***p*-value**	**95% CI**	r
Italy	Anxiety	sex	−1.21 (95)	0.23	[−13.31; 3.25]	
		Age	0.19 (95)	0.85	[−7.38; 8.93]	−0.03
	Avoidance	sex	2.19 (95)	0.03	[0.67; 13.12]	
		Age	−0.49 (95)	0.62	[−7.78; 4.69]	0.19
Singapore	Anxiety	sex	1.69 (214)	0.09	[−0.84; 10.80]	
		Age	−0.03 (214)	0.97	[−5.64; 5.45]	0.03
	Avoidance	sex	−0.21 (214)	0.83	[−5.39; 4.34]	
		Age	1.00 (214)	0.32	[−2.27; 6.92]	−0.07
Total	Anxiety	sex	0.54 (311)	0.59	[−3.50; 6.16]	
		Age	−0.14 (311)	0.89	[−5.27; 4.57]	−0.05
		Culture	3.24 (311)	0.13 *	[3.18; 13.02]	
	Avoidance	sex	0.81 (311)	0.42	[−2.29; 5.50]	
		Age	0.16 (311)	0.87	[−3.65; 4.30]	0.01
		Culture	2.56 (311)	0.01	[1.19; 9.18]	

Table 2.5: Summary of statistical values from Student's *t*-tests for sex and age over the ECR-R dependent variables anxiety and avoidance. Pearson correlation coefficients among each ECR-R variable and age are also reported. $^*p<.008$

The means and standard deviations of the continuous variables are shown in Table 2.3, and their intercorrelations were examined, as reported in Table 2.6, for the Italian and Singaporean sample, respectively, and in Table 2.7 for the total sample.

A six-step HMR was conducted separately on the Italian and Singaporean sample for each ECR-R subscale (namely anxiety and avoidance) as the DV (see Table 2.4). A seven-step HMR was conducted on the

subscale	**M_Care**	**M_Overp**	**F_Care**	**F_Overp**	**Anxiety**	**Avoidance**
M_Care		−0.29 ***	0.43 ***	−0.10	−0.06	−0.07
M_Overp	−0.31 *		−0.17	0.39 ***	0.1	0.05
F_Care	0.49 ***	−0.23		−0.18	−0.16	−0.09
F_Overp	−0.07	0.39 ***	−0.30 *		0.17	0.10
Anxiety	−0.36 **	0.42 ***	−0.37 **	0.20		0.38 ***
Avoidance	−0.25	0.19	−0.20	0.08	0.35 **	

Table 2.6: Pearson correlation coefficients and significance values among questionnaire subscales of the Italian and Singaporean samples separately. Values above the diagonal refer to the Singaporean sample, while values under the diagonal refer to the Italian sample. As regards the Italian sample, the PBI maternal care was square-transformed before the analysis. Significance is adjusted for multiple tests (corrected *alpha* = 0.003). *p<.003 **p<.001 ***p<.0001

subscale	**M_Care**	**M_Overp**	**F_Care**	**F_Overp**	**Anxiety**	**Avoidance**
M_Care						
M_Overp	-.29***					
F_Care	.43***	-.18*				
F_Overp	-.07	.40***	-.20**			
Anxiety	-.17*	.11	-.24***	.15		
Avoidance	-.12	.07	-.13	.07	.39***	

Table 2.7: Pearson correlation coefficients and significance values among questionnaire subscales of the total sample; significance is adjusted for multiple tests (corrected *alpha* = 0.003). *p<.003 **p<.001 ***p<.0001

total sample for each ECR-R subscale as the DV (see Table 2.4).

HMRs with the final step showing significant effects ($p < 0.025$) are explained below and reported in Table 2.8 for the Italian sample, in Table 2.11 for the Singaporean sample, and in Table 2.13 for the total sample. Otherwise, the explanation and tabulation of the results obtained from the HMRs not presenting significant effects ($p > 0.025$) at the final step are presented in the Tables 2.9, 2.10, 2.12.

2.3.2 Italian Sample

Anxiety

Table 2.8 represents the series of HMRs conducted on the ECR-R anxiety of the Italian sample (total sum of squares - SS = 38,793). At Step 1, *OXTR* explained a non-significant 1% of variance (F(1,95) = 0.62, residual sum of squares - RSS = 38,597, p= 0.43). Entering the maternal care variable at Step 2 explained a significant additional 13.3% of variance (F(1,94) = 16.35, RSS = 33,425, $p < 0.0001$). After introducing maternal overprotection at Step 3, both maternal care and maternal overprotection were positive predictors, accounting for a significant 10% of variance (F(1,93) = 12.55, RSS = 29,455, $p < 0.001$). The addition of the paternal care variable to the regression model (Step 4) justified a further significant 4% of variation in anxiety (F(1,92) = 4.85, RSS = 27,921, $p = 0.03$) given the main effects of maternal overprotection and maternal care. No significant change in the R^2 was observed when the final variable paternal overprotection was included at Step 5 (F(1,91) = 0.00, RSS = 27,921, $p = 0.99$). At Step 6, the hypothesized interaction between *OXTR* and paternal bonding dimensions on anxiety was tested ($f^2 = 0.39$, power = 0.99). Here, a main effect of maternal overprotection was found ($\beta = 1.11$, SE = 0.46, $t = 2.40$, $p < 0.02$). Although the final model computed the highest proportion of explained variance in anxiety by the model ($R^2 = 0.29$), no significant difference was detected compared to the previous step (F(1,91) = 0.32, RSS = 27,517, $p = 0.87$). As indicated in Table 2.6, maternal overprotection was also found positively associated with adult anxiety ($t = 4.46$, df = 95, $r = 0.42$, $p < 0.0001$) (Figure 1). Specifically, the two-tailed post hoc Welch's t test ($\alpha = 0.05$) revealed that felt anxiety towards the partner was significantly different between participants who experienced low levels in maternal overprotection compared to those who had a past of maternal overprotection ($t = -2.31$, df = 71.3, $p = 0.024$, $d = -0.49$) (Figure 1). Contrary to *HP1*, no main effect of genotype or interactions between covariates and genotype were identified.

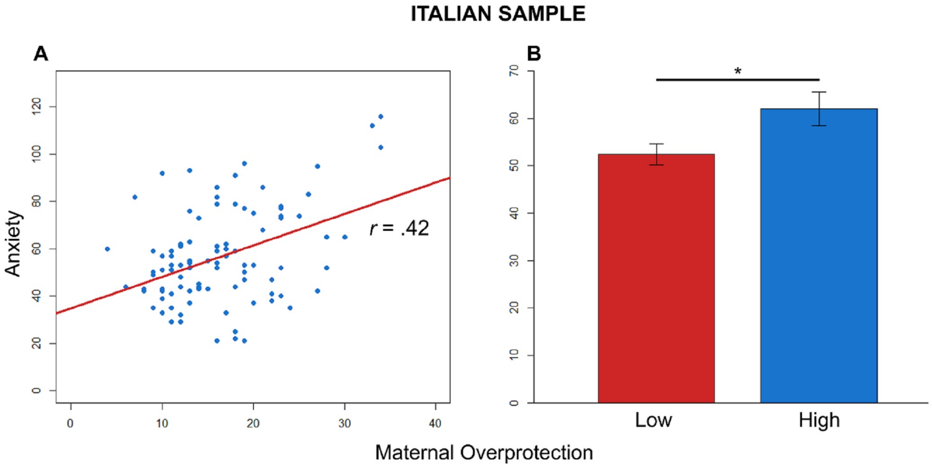

Figure 1: Effect on anxiety for the Italian sample. (**A**) Effect of early maternal overprotection on adult anxiety. Correlation between the scores of anxiety and maternal overprotection. Blue circles = Italian participants. The red line represents the linear model for the Italian participants. The r-value refers to Pearson's r correlation. (**B**) Comparison between the scores of ECR-R anxiety in low and high maternal overprotection (* p ¡ 0.025).

Step	**Variable**	β	**SE**	t	R	R^2	Δ R^2
1					.07	.01	.01
	OXTR rs53576	2.84	4.09	0.69			
2					.37	.14	.13***
	OXTR rs53576	3.11	3.83	0.81			
	M_Care	-0.02***	0.01	-3.81			
3					.49	.24	.10***
	OXTR rs53576	3.36	3.62	0.93			
	M_Care	-0.01**	0.01	-2.73			
	M_OverP	1.08***	0.30	3.54			
4					.53	.28	.04*
	OXTR rs53576	4.06	3.55	1.14			
	M_Care	-0.01	0.01	-1.46			
	M_OverP	1.01**	0.30	3.39			
	F_Care	-0.50*	0.22	-2.25			
5					.53	.28	0
	OXTR rs53576	4.06	3.57	1.14			
	M_Care	-0.01	0.01	-1.42			
	M_OverP	1.01**	0.33	3.11			
	F_Care	-0.50*	0.23	-2.13			
	F_OverP	0.00	0.29	0.00			
6					.54	.29	.01
	OXTR rs53576	18.08	17.73	1.02			
	M_Care	-0.01	0.01	-0.72			
	M_OverP	1.12*	0.47	2.40			
	F_Care	-0.48	0.38	-1.29			
	F_OverP	0.20	0.44	0.45			
	OXTR rs53576 x M_Care	0.00	0.01	-0.34			
	OXTR rs53576 x M_OverP	-0.26	0.67	-0.39			
	OXTR rs53576 x F_Care	-0.01	0.49	-0.01			
	OXTR rs53576 x F_OverP	-0.46	0.61	0.76			

Table 2.8: Hierarchical multiple regression on ECR-R anxiety for the Italian sample. Note. SE = standard error of unstandardized coefficient. *p<.05; **p<.01; ***p<.001.

Avoidance

Table S2.9 illustrates the series of hierarchical multiple regression conducted on ECR-R avoidance for the Italian sample (total SS = 22689). At step 1, adding OXTR to the model explained a non-significant 1% of variance ($F(1,95) = 0.70$, RSS = 22540, $p = .41$). At step 2, maternal care contributed significantly to the model and accounted for 6% of the variation in avoidance ($F(1,94) = 6.70$, RSS = 21122, $p < .01$). At step 3, the addition of maternal overprotection increased the model non-significantly by 1% ($F(1,93) = 1.49$, RSS = 20807, $p = .23$), although maternal care was still identified as positive predictor. Paternal care was entered at step 4, but no change in the $\mathbf{R}^2$ was observed ($F(1,92) = 0.53$, RSS = 20695, $p = .47$). No significant increase in the $\mathbf{R}^2$ was not even found when the variable paternal overprotection was included at step 5 ($F(1,91) = 0.01$, RSS = 20693, $p = .93$). At step 6, the hypothesized interaction between OXTR and paternal bonding subscales on avoidance was tested ($f^2 = .22$, power = .94). The final model estimates the highest proportion of explained variance in avoidance by the model ($R^2 = .19$) with a significant further 10% ($F(4,87) = 2.68$, RSS = 18422, $p < .04$). Here, the slight effect of maternal care did not reach the significance after multiple tests' correction ($\beta = -0.02$, SE = 0.01, $t = -2.26$, $p < .03$).

2.3.3 Singaporean Sample

Anxiety

Table S2.10 shows the series of hierarchical multiple regression conducted on ECR-R anxiety of the Singaporean sample (total SS = 91312). The introduction of OXTR at step 1 did not increase the explained variation of the model ($F(1,214) = 0.38$, RSS = 91158, $p = .54$). Maternal care was entered at step 2 and a not significant 1% of variance was detected ($F(1,213) = 0.96$, RSS = 90771, $p = .33$). No variation in $\mathbf{R}^2$ was found at step 3, when maternal overprotection was included ($F(1,212) = 0.01$,

Step	**Variable**	β	**SE**	t	R	**R**^{2}	Δ **R**^{2}
1					.08	.01	.01
	OXTR rs53576	-2.47	3.13	-0.79			
2					.26	.07	.06*
	OXTR rs53576	-2.33	3.05	-0.77			
	M_Care	-0.01*	0.00	-2.51			
3					.29	.08	.01
	OXTR rs53576	-2.26	3.04	-0.74			
	M_Care	-0.01*	0.00	-2.02			
	M_OverP	0.30	0.26	1.19			
4					.30	.09	.01
	OXTR rs53576	-2.07	3.06	-0.68			
	M_Care	-0.01	0.01	-1.47			
	M_OverP	0.29	0.26	1.11			
	F_Care	-0.14	0.19	-0.71			
5					.30	.09	0
	OXTR rs53576	-2.07	3.08	-0.67			
	M_Care	-0.01	0.01	-1.42			
	M_OverP	0.30	0.28	1.05			
	F_Care	-0.14	0.20	-0.70			
	F_OverP	-0.02	0.25	-0.09			
6					.43	.19	.10*
	OXTR rs53576	-18.31	14.51	-1.26			
	M_Care	-0.02*	0.01	-2.26			
	M_OverP	0.04	0.38	0.10			
	F_Care	-0.21	0.31	-0.69			
	F_OverP	0.37	0.36	1.05			
	OXTR rs53576 x M_Care	0.02	0.01	1.82			
	OXTR rs53576 x M_OverP	0.44	0.55	0.80			
	OXTR rs53576 x F_Care	0.29	0.40	0.72			
	OXTR rs53576 x F_OverP	-0.81	0.50	-1.63			

Table 2.9: Hierarchical multiple regression on ECR-R avoidance for the Italian sample. Note. SE =standard error of unstandardized coefficient. *p<.05

RSS = 90769, p= .95). At step 4, paternal care in input motivated a significant change in $\mathbf{R}^2$ (F(1,211) = 4.65, RSS = 88901, p= .03) and disclosed a main effect of the same PBI dimension on anxiety. At step 5, paternal overprotection was entered and accounted for a significant 2% of additional variance (F(1,210) = 6.35, RSS = 86349, p= .01). At this level, only paternal overprotection was a positive predictor of anxiety. At step 6, the hypothesized interaction between OXTR and paternal bonding dimensions on anxiety was verified (f^2 = .10, power = 0.95). Although most of the variance in anxiety (R^2 = .09) depended on the final model, no significant difference between step 6 and 5 was discovered (F(4,206) = 2.21, RSS = 82799, p= .07). Considering the application of multiple tests' correction, the interaction effect between OXTR and maternal overprotection on the anxiety levels did not reach an acceptable significance level at the final step (β = -1.06, SE = 0.49, t = -2.17,

p= .03).

Step	**Variable**	β	**SE**	t	R	R^2	Δ R^2
1					.04	.00	.00
	OXTR rs53576	-1.75	2.91	-0.60			
2					.08	.01	.01
	OXTR rs53576	-1.95	2.92	-0.67			
	M_Care	-0.19	0.20	-0.95			
3					.08	.01	.00
	OXTR rs53576	-1.93	2.93	-0.66			
	M_Care	-0.20	0.21	-0.93			
	M_OverP	-0.01	0.21	-0.07			
4					.16	.03	.02*
	OXTR rs53576	-1.32	2.95	-0.45			
	M_Care	0.00	0.23	-0.01			
	M_OverP	-0.04	0.21	-0.19			
	F_Care	-0.40*	0.19	-2.11			
5					.23	.05	.02*
	OXTR rs53576	-1.44	2.89	-0.50			
	M_Care	-0.05	0.23	-0.20			
	M_OverP	-0.25	0.22	-1.11			
	F_Care	-0.33	0.19	-1.75			
	F_OverP	0.57*	0.23	2.49			
6					.31	.09	.04
	OXTR rs53576	-0.59	15.61	-0.04			
	M_Care	-0.66	0.41	-1.60			
	M_OverP	0.54	0.41	1.32			
	F_Care	0.08	0.35	0.22			
	F_OverP	0.31	0.39	0.80			
	OXTR rs53576 x M_Care	0.81	0.49	1.64			
	OXTR rs53576 x M_OverP	-1.06*	0.49	-2.17			
	OXTR rs53576 x F_Care	-0.45	0.42	-1.09			
	OXTR rs53576 x F_OverP	0.30	0.48	0.62			

Table 2.10: Hierarchical multiple regression on ECR-R anxiety for the Singaporean sample. Note. SE =standard error of unstandardized coefficient. *p<.05

Avoidance

Table 2.11 presents the series of HMRs performed on ECR-R avoidance for the Singaporean sample (total SS = 63,074). Entering at Step 1 the only genetic variable did not increase the explained portion of variance (F(1,214) = 0.18, RSS = 63,021, p = 0.67). At Step 2, maternal care was added to the regression model and accounted for a non-significant 1% of additional variance (F(1,213) = 0.99, RSS = 62,733, p = 0.32). The inclusion of maternal overprotection at Step 3 did not further improve the value of $\mathbf{R}^2$ (F(1,212) = 0.15, RSS = 62,689, p = 0.70). No change in the explained variance was even observed when introducing the paternal care dimension at Step 4 ($F(1{,}211) = 0.87$, RSS = 62,438, $p = 0.35$). At Step 5, the addition of the subscale paternal overprotection justified an increased 1% of variation in avoidance, which was not significant ($F(1{,}210) = 1.59$, RSS = 61,976, $p = 0.21$). At Step 6, the hypothesized (*HP2*) interaction between *OXTR* and paternal bonding dimensions on avoidance was tested ($f^2 = 0.05$, power = 0.67). The final model maximized the explained variance ($R^2 = 0.05$), but no significant difference was found compared to the previous step ($F(4{,}206) = 1.74$, RSS = 59,956, $p = 0.14$).

Step	**Variable**	β	**SE**	t	R	R^2	ΔR^2
1					.03	.00	.00
	OXTR rs53576	1.02	2.42	0.43			
2					.07	.01	.01
	OXTR rs53576	0.86	2.42	0.35			
	M_Care	-0.17	0.17	-0.99			
3					.08	.01	.00
	OXTR rs53576	0.78	2.44	0.32			
	M_Care	-0.15	0.18	-0.84			
	M_OverP	0.07	0.17	0.38			
4					.10	.01	.00
	OXTR rs53576	1.00	2.45	0.41			
	M_Care	-0.08	0.19	-0.39			
	M_OverP	0.06	0.18	0.33			
	F_Care	-0.15	0.16	-0.92			
5					.13	.02	.01
	OXTR rs53576	0.95	2.45	0.39			
	M_Care	-0.09	0.19	-0.49			
	M_OverP	-0.03	0.19	-0.16			
	F_Care	-0.12	0.16	-0.73			
	F_OverP	0.24	0.19	1.25			
6					.22	.05	.03
	OXTR rs53576	-17.16	13.28	-1.29			
	M_Care	-0.83*	0.35	-2.37			
	M_OverP	0.14	0.35	0.40			
	F_Care	0.22	0.29	0.76			
	F_OverP	0.02	0.33	0.05			
	OXTR rs53576 x M_Care	1.03*	0.42	2.45			
	OXTR rs53576 x M_OverP	-0.16	0.42	-0.39			
	OXTR rs53576 x F_Care	-0.45	0.35	-1.27			
	OXTR rs53576 x F_OverP	0.30	0.41	0.73			

Table 2.11: Hierarchical multiple regression on ECR-R avoidance for the Singaporean sample. Note. SE =standard error of unstandardized coefficient. *$p<.05$

At this final step, early maternal care was the strongest predictor of adult avoidance ($\beta = -0.83$, SE = 0.35, $t = -2.37$, $p < 0.02$). As reported in Table 2.6, the negative correlation between maternal care and adult avoidance was not significant ($t = -1.02$, df = 214, $r = -0.07$, p

= 0.30) (Figure 2). Specifically, the two-tailed post hoc Student's t test (α = 0.05) showed that avoidance towards the partner was not significantly different between participants who reported low and high scores in maternal care (t = 0.78, df = 214, p = 0.44, d= 0.11) (Figure 2).

The significant two-way interaction between rs53576 and maternal overprotection also emerged for adult avoidance (β = −0.83, SE = 0.35, t = −2.37, p < 0.02). The distribution of genotypes A/A vs. G-carriers was not significantly different between high vs. low maternal care (X^2 (1) = 1.19, p = 0.028). Maternal care was positively associated with avoidance for G-carriers (t = 0.51, df = 134, r = 0.04, p = 0.61), but negatively associated with avoidance for A/A homozygotes (t = −2.38, df = 78, r = −0.26, p = 0.02), as predicted by *HP2* (Figure 2). Although only one Pearson's r was significant, Fisher's z test confirmed that the difference between the slopes for A/A and G-carriers was significant (z = −2.14, p = 0.03). The one-tailed post hoc Student's t test (corrected α = 0.025) revealed that adult avoidance was not significantly different between A/A- and G-carriers when they experienced a history of low maternal caregiving (t = −1.01, df = 107, p = 0.84, d= −0.21) (Figure 2).

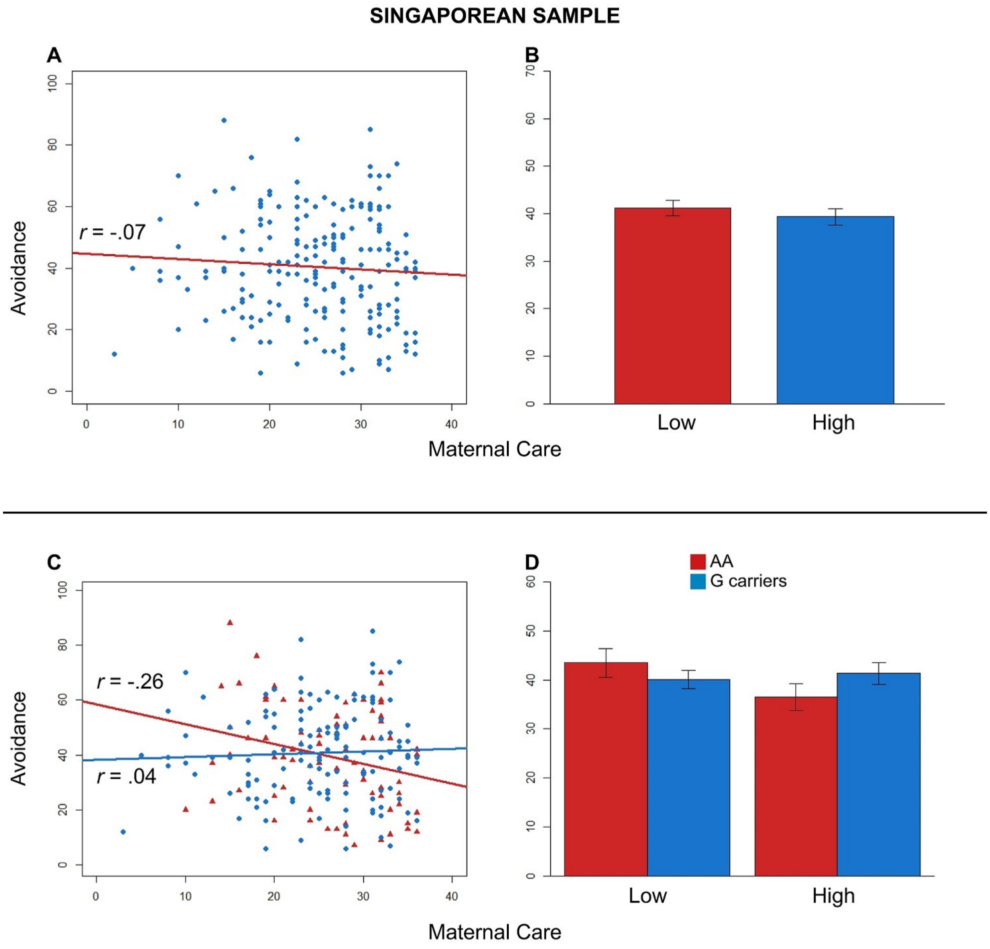

Figure 2: Effects on avoidance for the Singaporean sample. (**A**) Effect of early maternal care on adult avoidance. Correlation between the reported avoidance and maternal care. Blue circles = Singaporean participants. The red line represents the linear model for the Singaporean participants. (**B**) Comparison between the scores of ECR-R avoidance in low and high maternal care. (**C**) Effect of the interaction between genotype and early maternal care on adult avoidance. Correlations between the scores of anxiety and the recalled maternal care. Red triangles = A/A; blue circles = G-carriers. Lines depict the linear models for A/A homozygotes (red) and G-carriers (blue). (**D**) Contrast between the scores of ECR-R avoidance in A/A homozygotes (red) and G-carriers (blue) divided into low and high maternal care. r-values refer to Pearson's r correlations for both (**A**,**C**).)

2.3.4 Total Sample: Italian and Singaporean Participants

Anxiety

Table 2.12 reports the series of hierarchical multiple regression performed on ECR-R anxiety of the total sample (total SS = 134493). At step 1, culture was considered as starting variable of the regression model, explaining a significant 3% of the total variance (F(1,311) = 11.67, RSS = 130105, p= .0007). Culture was significant at this step, as positive predictor. When entering OXTR at step 2, no variation in R^2 was observed (F(2,309) = 0.22, RSS = 129940, p< .80), but culture still obtained a significant effect. The addition of maternal care to the model at step 3 increased the variance of a significant 3% (F(1,308) = 9.12, RSS = 126510, p< .003). Both culture and maternal care were positive predictors at this step.

At step 4, although maternal overprotection improved the model by a non-significant 1% of variation in anxiety (F(1,307) = 2.52, RSS = 125561, p= .11), culture and maternal care were still the strongest predictors of the model. Paternal care contributed significantly in explaining a further 3% of variance at step 5 (F(1,306) = 9.63, RSS = 121937, p= .002). Here, culture and paternal care best predict participants' anxiety. At step 6, the parental overprotection dimension was introduced and accounted for a significant 2% of variance (F(1,305) = 5.01, RSS = 120053, p= .026). At this step, the three variable culture, paternal care and paternal overprotection resulted significant predictors. At step 7, the hypothesized interaction between culture, gene and paternal bonding dimensions on anxiety was explored (f^2 = .09, power = .98). The final model computed the highest proportion of explained variance in anxiety by the model (R^2 = .21), as highlighted by the significant increase of R^2 (F(22,283) = 1.64, RSS = 106451, p= .036). From the overall interactive model, no significant main effects of culture, genotype or caregiving behavior as well as two-way or three-way interactions were found for adult anxiety.

Avoidance

Table 2.13 reports the series of HMRs performed on ECR-R avoidance for the total sample (total SS = 87,563). The regression revealed that at

Step	**Variable**	β	**SE**	***t***	***R***	**R^2**	**Δ R^2**
1					.18	.03	.03***
	Culture	8.10**	2.50	3.24			
2					.18	.03	.00
	Culture	7.56**	2.65	2.85			
	OXTR rs53576 A/G-A/A	-0.64	2.80	-0.23			
	OXTR rs53576 G/G-A/A	-1.96	3.19	-0.61			
3					.24	.06	.03**
	Culture	7.01**	2.63	2.67			
	OXTR rs53576 A/G-A/A	-1.02	2.77	-0.37			
	OXTR rs53576 G/G-A/A	-2.48	3.16	-0.78			
	M_Care	-0.44**	0.15	-2.89			
4					.26	.07	.01
	Culture	7.27**	2.63	2.77			
	OXTR rs53576 A/G-A/A	-1.22	2.77	-0.44			
	OXTR rs53576 G/G-A/A	-3.04	3.17	-0.96			
	M_Care	-0.37*	0.16	-2.32			
	M_OverP	0.27	0.18	1.52			
5					.31	.09	.03**
	Culture	6.90**	2.60	2.66			
	OXTR rs53576 A/G-A/A	-0.47	2.74	-0.17			
	OXTR rs53576 G/G-A/A	-1.90	3.16	-0.60			
	M_Care	-0.16	0.17	-0.93			
	M_OverP	0.23	0.18	1.29			
	F_Care	-0.45**	0.15	-3.02			
6					.33	.11	.02*
	Culture	7.82**	2.61	2.99			
	OXTR rs53576 A/G-A/A	-0.18	2.73	-0.07			
	OXTR rs53576 G/G-A/A	-1.77	3.14	-0.56			
	M_Care	-0.21	0.17	-1.19			
	M_OverP	0.07	0.19	0.37			
	F_Care	-0.39*	0.15	-2.55			
	F_OverP	0.41*	0.19	2.19			
7					.46	.21	.10*
	Culture	36.09	33.32	1.08			
	OXTR rs53576 A/G-A/A	20.05	35.92	0.56			
	OXTR rs53576 G/G-A/A	37.17	34.54	1.08			
	M_Care	-0.01	1.02	-0.02			
	M_OverP	4.00	2.05	1.95			
	F_Care	-1.45	0.89	-1.62			
	F_OverP	-0.53	1.05	-0.50			
	Culture x OXTR rs53576 A/G-A/A	-17.77	39.35	-0.45			
	Culture x OXTR rs53576 G/G-A/A	-46.96	40.14	-1.17			
	Culture x M_Care	-0.64	1.09	-0.59			
	Culture x M_OverP	-3.46	2.09	-1.66			
	Culture x F_Care	1.53	0.95	1.60			
	Culture x F_OverP	0.84	1.12	0.76			
	OXTR rs53576 A/G-A/A x M_Care	-0.05	1.16	-0.04			
	OXTR rs53576 G/G-A/A x M_Care	-0.42	1.07	-0.39			
	OXTR rs53576 A/G-A/A x M_OverP	-2.87	2.15	-1.34			
	OXTR rs53576 G/G-A/A x M_OverP	-3.12	2.11	-1.48			
	OXTR rs53576 A/G-A/A x F_Care	0.83	1.03	0.81			
	OXTR rs53576 G/G-A/A x F_Care	0.94	0.95	0.98			
	OXTR rs53576 A/G-A/A x F_OverP	0.36	1.27	0.28			
	OXTR rs53576 G/G-A/A x F_OverP	0.28	1.15	0.24			
	Culture x OXTR rs53576 A/G-A/A x M_Care	1.07	1.27	0.84			
	Culture x OXTR rs53576 G/G-A/A x M_Care	0.93	1.23	0.75			
	Culture x OXTR rs53576 A/G-A/A x M_OverP	1.57	2.20	0.71			
	Culture x OXTR rs53576 G/G-A/A x M_OverP	2.77	2.21	1.25			
	Culture x OXTR rs53576 A/G-A/A x F_Care	-1.54	1.11	-1.38			
	Culture x OXTR rs53576 G/G-A/A x F_Care	-1.03	1.08	-0.95			
	Culture x OXTR rs53576 A/G-A/A x F_OverP	0.07	1.36	0.05			
	Culture x OXTR rs53576 G/G-A/A x F_OverP	-0.49	1.32	-0.37			

Table 2.12: Hierarchical multiple regression on ECR-R anxiety for the total sample. Note. SE =standard error of unstandardized coefficient. *$p<.05$ **$p<.01$ ***$p<.001$

Stage 1, culture contributed significantly to the model explaining the first 2% of variance ($F(1{,}311) = 6.90$, RSS = 85,763, $p = 0.009$). Culture was significant at this step, as a positive predictor. At Step 2, introducing the genetic factor did not increase the variance of avoidance ($F(2{,}309)$

= 0.03, RSS = 85,745, p = 0.97), but a main effect of culture was still present. At Step 3, maternal care was added to the regression model and accounted for a significant 1% of additional variance (F(1,308) = 4.42, RSS = 84,592, p = 0.04). Here, the variable culture and the novel variable maternal care were the strongest predictors. At Step 4, the improvement of 1% of variation in avoidance due to the inclusion of maternal overprotection in the model was not significant (F(1,307) = 1.03, RSS = 84,325, p = 0.31). Only culture was a positive predictor at this stage. No change in the explained variance was observed when introducing the paternal care dimension at Step 5 (F(1,306) = 1.79, RSS = 83,858, p = 0.18). Culture was still a strong predictor at this stage. The addition of the paternal overprotection variable to the regression model at Step 6 justified 1% of the variation in avoidance which did not result in being statistically significant F(1,305) = 1.11, RSS = 83,569, p = 0.29). However, a significant main effect of culture was identified at this stage. Finally, at Step 7, the potential interaction between culture, *OXTR*, and PBI dimensions on avoidance (*H3*) was inspected (f^2 = 0.17, power = 0.99). This interactive model increased the explained variance (R^2 = 0.16) significantly from the previous step (F(22,283) = 1.70, RSS = 73,827, p = 0.028).

At this last step, one one-way effect, three two-way interaction effects, and two three-way interaction effects were found.

Firstly, early maternal overprotection singularly predicted adult avoidance (β = 5.03, SE = 1.71, t = 2.95, $p < 0.004$). As evident from Table 2.7, the positive correlation between maternal overprotection and adult avoidance was not significant ($t = -1.26$, df = 311, r = 0.07, p = 0.21) (Figure 3A; blue circles = Italian and Singaporean participants merged; the red line represents the linear model for all the participants). The two-tailed post hoc Student's t test (α = 0.05) showed that avoidance towards the partner was not significantly different between participants who reported low and high scores in maternal overprotection ($t = -1.27$, df = 311, p = 0.21, $d = -0.14$) (Figure 3B).

The main effect of paternal care ($p > 0.025$) did not survive the magnitude of the Bonferroni correction (corrected $alpha = 0.025$).

As concerns the interaction effects, the significant two-way interaction between culture and maternal overprotection also emerged for avoidance ($\beta = -4.89$, SE $= 1.74$, $t = -2.81$, $p = 0.005$). Maternal overprotection positively correlated with the avoidance reported by both Italian ($t = 1.91$, df $= 95$, $r = 0.19$, $p = 0.06$) and Singaporean participants ($t = 0.69$, df $= 214$, $r = 0.05$, $p = 0.49$) (Figure 3C; red triangles = Italian participants; blue circles = Singaporean participants; lines depict the linear models for Italian (red) and Singaporean (blue) participants). However, the slopes for Italians and Singaporeans were not significantly different ($z = 1.15$, $p = 0.13$). The exploratory two-tailed Student's t test (corrected $alpha = 0.025$) revealed that adult avoidance was significantly different between Italian and Singaporean participants when they experienced a history of low maternal overprotection ($t = -2.91$, df $=$ 162, $p = 0.004$, d=-0.51) (Figure 3D), but not when they had a past of high maternal overprotection ($t = -0.88$, df $= 147$, $p = 0.38$, $d = -0.15$).

The two-way interaction between culture and paternal care ($p > 0.025$) was not considered significant once *alpha* correction was applied to the linear models (corrected $alpha = 0.025$).

Two further significant two-way interactions between *OXTR* levels and maternal overprotection on adult avoidance were detected (A/G-A/A: $\beta = -5.27$, SE $= 1.71$, $t = -2.96$, $p = 0.003$; G/G-A/A: $\beta = -4.57$, SE $=$ 1.76, $t = -2.59$, $p = 0.009$). The distribution of genotypes A/A vs. A/G vs. G/G was not significantly different between high vs. low maternal overprotection (X^2 (2) $= 3.75$, $p = 0.15$). Maternal overprotection was positively associated with avoidance for A/A ($t = 1.32$, df $= 92$, $r =$ 0.14, $p = 0.19$) and G/G homozygotes ($t = 1.91$, df $= 88$, $r = 0.20$, $p = 0.06$), but not for the heterozygotes ($t = -0.31$, df $= 127$, $r = -0.03$, $p = 0.75$) (Figure 3E; red triangles = A/A; green squares = A/G; blue circles = G/G; lines represent the linear models for A/A homozygotes (red), A/G (green), and G/G (blue)). No difference between the slopes

Step	**Variable**	β	**SE**	t	R	R^2	ΔR^2
1					.14	.02	.02**
	Culture	5.19*	2.03	2.55			
2					.14	.02	.00
	Culture	5.05*	2.15	2.35			
	OXTR rs53576 A/G-A/A	0.21	2.27	0.09			
	OXTR rs53576 G/G-A/A	-0.39	2.59	-0.15			
3					.18	.03	.01*
	Culture	4.74*	2.15	2.21			
	OXTR rs53576 A/G-A/A	-0.01	2.27	-0.01			
	OXTR rs53576 G/G-A/A	-0.69	2.58	-0.27			
	M_Care	-0.26*	0.13	-2.05			
4					.19	.04	.01
	Culture	4.88*	2.15	2.27			
	OXTR rs53576 A/G-A/A	-0.12	2.27	-0.05			
	OXTR rs53576 G/G-A/A	-0.99	2.60	-0.38			
	M_Care	-0.22	0.13	-1.67			
	M_OverP	0.14	0.15	0.99			
5					.21	.04	.00
	Culture	4.75*	2.15	2.20			
	OXTR rs53576 A/G-A/A	0.15	2.28	0.07			
	OXTR rs53576 G/G-A/A	-0.58	2.62	-0.22			
	M_Care	-0.14	0.14	-0.99			
	M_OverP	0.13	0.15	0.88			
	F_Care	-0.16	0.12	-1.31			
6					.21	.05	.01
	Culture	5.11*	2.18	2.34			
	OXTR rs53576 A/G-A/A	0.26	2.28	0.12			
	OXTR rs53576 G/G-A/A	-0.53	2.62	-2.20			
	M_Care	-0.16	0.15	-1.11			
	M_OverP	0.07	0.16	0.42			
	F_Care	-0.14	0.13	-1.08			
	F_OverP	0.16	0.16	1.03			
7					.40	.16	.11*
	Culture	11.02	27.75	0.40			
	OXTR rs53576 A/G-A/A	14.40	29.92	0.48			
	OXTR rs53576 G/G-A/A	-14.19	28.76	-0.49			
	M_Care	-0.73	0.85	-0.87			
	M_OverP	5.03**	1.71	2.95			
	F_Care	-1.52*	0.75	-2.04			
	F_OverP	-1.71	0.87	-1.96			
	Culture x OXTR rs53576 A/G-A/A	-27.14	32.77	-0.83			
	Culture x OXTR rs53576 G/G-A/A	-12.77	33.42	-0.38			
	Culture x M_Care	-0.10	0.91	-0.11			
	Culture x M_OverP	-4.89**	1.74	-2.81			
	Culture x F_Care	1.74*	0.80	2.19			
	Culture x F_OverP	1.73	0.93	1.87			
	OXTR rs53576 A/G-A/A x M_Care	0.04	0.97	0.05			
	OXTR rs53576 G/G-A/A x M_Care	0.78	0.89	0.87			
	OXTR rs53576 A/G-A/A x M_OverP	-5.27**	1.79	-2.96			
	OXTR rs53576 G/G-A/A x M_OverP	-4.57**	1.76	-2.59			
	OXTR rs53576 A/G-A/A x F_Care	1.25	0.86	1.46			
	OXTR rs53576 G/G-A/A x F_Care	1.60*	0.80	2.01			
	OXTR rs53576 A/G-A/A x F_OverP	2.18*	1.06	2.06			
	OXTR rs53576 G/G-A/A x F_OverP	1.27	0.96	1.33			
	Culture x OXTR rs53576 A/G-A/A x M_Care	1.24	1.06	1.17			
	Culture x OXTR rs53576 G/G-A/A x M_Care	-0.11	1.03	-0.11			
	Culture x OXTR rs53576 A/G-A/A x M_OverP	4.91**	1.83	2.67			
	Culture x OXTR rs53576 G/G-A/A x M_OverP	4.79**	1.84	2.61			
	Culture x OXTR rs53576 A/G-A/A x F_Care	-2.06*	0.93	-2.22			
	Culture x OXTR rs53576 G/G-A/A x F_Care	-1.44	0.90	-1.60			
	Culture x OXTR rs53576 A/G-A/A x F_OverP	-1.88	1.13	-1.66			
	Culture x OXTR rs53576 G/G-A/A x F_OverP	-1.09	1.10	-0.99			

Table 2.13: Hierarchical multiple regression on ECR-R avoidance for the total sample. Note. SE = standard error of unstandardized coefficient. *p<.05 **p<.01

for A/A and A/G ($z = -1.24$, $p = 0.21$), for A/A and G/G ($z = -0.44$, $p = 0.66$), and for A/G and G/G ($z = -1.67$, $p = 0.09$) was observed. In the only condition of high maternal overprotection (corrected $\alpha = 0.017$), the exploratory two-tailed post hoc Student's t tests proved that adult avoidance was not significantly different between A/A and A/G (t = 1.34, df = 97, p = 0.18, d= 0.28), A/A and G/G (t = 0.58, df = 87, p = 57, d= 0.12), and A/G and G/G (t = 0.90, df = 108, p = 37, d= 0.17) (Figure 3F).

Considerably, the two two-way interaction respectively between *OXTR* and paternal care and between *OXTR* and paternal overprotection on adult avoidance did not fall below the level of acceptability ($p > 0.025$). Concerning the potential three-way interaction expected for the observational *HP3*, two significant three-way interactions between culture, *OXTR* levels, and maternal overprotection on adult avoidance were discovered (A/G-A/A: $\beta = 4.91$, SE = 1.83, $t = 2.67$, $p < 0.008$; G/G-A/A: $\beta = 4.79$, SE = 1.84, $t = 2.61$, $p = 0.009$). In the Italian group, maternal overprotection was positively associated with avoidance for all the genetic groups (A/A: $t = 1.86$, df = 12, $r = 0.48$, $p = 0.09$; A/G: $t = 1.39$, df = 33, $r = 0.24$, $p = 0.17$; G/G: $t = 0.73$, df = 46, $r = 0.11$, $p = 0.47$) (Figure 3G; red triangles = A/A; green squares = A/G; blue circles = G/G; lines show the linear models for A/A homozygotes ((red), A/G (green), and G/G (blue)). No difference between the slopes for all the Italian genetic groups was found (A/A-A/G: $z = 0.80$, $p = 0.21$); A/A-G/G: z = 1.23, $p = 0.11$; A/G-G/G: $z = 0.58$, $p = 0.28$). In the Singaporean group, maternal overprotection was positively associated with avoidance for A/A ($t = 0.90$, df = 78, $r = 0.10$, $p = 0.37$) and G/G ($t = 1.59$, df = 40, $r = 0.24$, $p = 0.12$), but the same PBI dimension was negatively associated with avoidance for A/G ($t = -0.85$, df = 92, $r = -0.09$, p = 0.40) (Figure 3H; red triangles = A/A; green squares = A/G; blue circles = G/G; lines show the linear models for A/A homozygotes (red), A/G (green), and G/G (blue)). Fisher's z-tests confirmed a significant difference between slopes for the A/G-G/G groups ($z = 1.75$, $p = 0.04$), but not for the A/A-A/G ($z = 1.23$, $p = 0.11$) and the A/A-G/G ($z = -0.74$, $p = 0.23$) groups.

In the condition of low maternal overprotection, the two-tailed post hoc Student's t tests (corrected $alpha$ = 0.025) confirmed that adult avoidance was not significantly different between A/A and G/G both in the Italian ($t = -0.36$, df = 30, $p = 0.72$, d=-0.15) and Singaporean group ($t = 0.74$, df = 61, $p = 0.47$, d= 0.21) (Figure 3I). Likewise, in the condition of high maternal overprotection (corrected $alpha = 0.025$), adult avoidance was not significantly different between A/A and G/G both in the Italian ($t = 2.28$, df = 28, $p = 0.03$, d= 1.04) and Singaporean group ($t = -0.94$, df = 57, $p = 0.35$, d=-0.25) (Figure 3J).

Nevertheless, the last three-way interaction between culture, *OXTR*, and paternal care approached, but did not reach significance ($p > 0.025$).

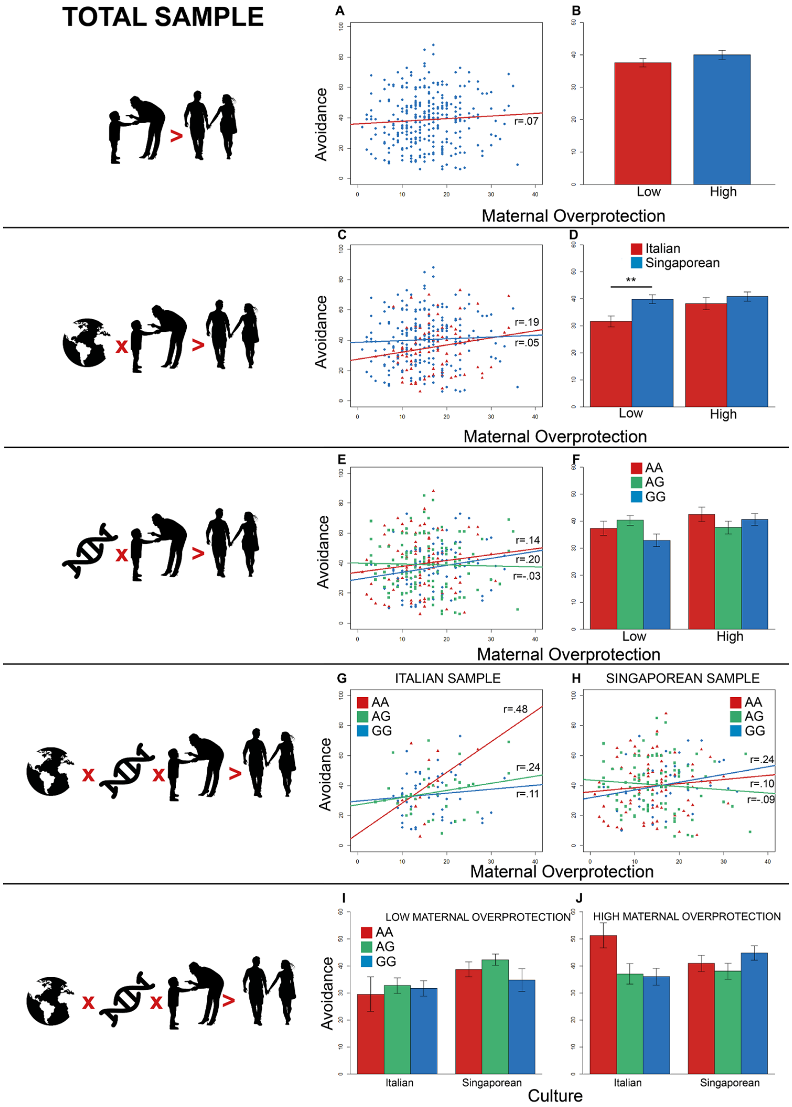

Figure 3: Effects on avoidance for the total sample. (**A**) Effect of early maternal overprotection on adult avoidance. (**B**) Comparison between the scores of ECR-R avoidance in low and high maternal overprotection. (**C**) Effect of the interaction between culture and early maternal overprotection on adult avoidance. (**D**) Contrast between the scores of ECR-R avoidance in Italian (red) and Singaporean (blue) groups. (**E**) Effect of the interaction between genotype and early maternal overprotection on adult avoidance. (**F**) Contrast between the scores of ECR-R avoidance in A/A homozygotes (red), A/G heterozygotes (green), and G/G homozygotes (blue) divided into low and high maternal overprotection. (**G**) Effect of the interaction between genotype and early maternal overprotection on adult avoidance for the Italian participants. (**H**) Effect of the interaction between genotype and early maternal overprotection on adult avoidance for the Singaporean participants. (**I**) Comparison between the scores of ECR-R avoidance in A/A homozygotes (red), A/G heterozygotes (green), and G/G homozygotes (blue) divided into Italian and Singaporean participants for low maternal overprotection. (**J**) Contrast between the scores of ECR-R avoidance in A/A homozygotes (red), A/G heterozygotes (green), and G/G homozygotes (blue) divided into Italian and Singaporean participants for high maternal overprotection. r-values refer to Pearson's r correlations. (** $p < 0.025$).

2.4 Discussion

Early interactions have been widely proven to have a crucial role in shaping psychological mechanisms that drive social interactions later in life. However, it is fundamental to take into account several factors that occur in the development of these psychosocial processes, such as genetic and cultural contributions. Starting from the evidence in the literature suggesting the key role of oxytocin (Ebstein et al., 2009, 2012) and parental bonding in influencing social behavior (Feeney, 2002), the main purpose of this study was to examine the effects of the different genetic susceptibility and early interactions on the levels of anxiety and avoidance experienced in adult relationships in two different cultural contexts. Within this multicultural framework, the Italian and Singaporean samples were respectively considered as representative of a Western-dominant culture and an Eastern-dominant culture. Specifically, we focused on recalled parental bonding, assessed in terms of parental care and overprotection. According to the information on the mean and median of each subscale (see Table 2.3), while parental dimensions did not diverge between the two cultural groups, anxiety and avoidance experienced in adult relationships showed different means and median values in the two populations. ECR-R has been translated into and validated in other languages and used for investigations in Eastern countries, proving good internal validity. At the same time, the few studies that adopted ECR-R for cross-cultural comparisons (Hao et al., 2019; Mastrotheodoros et al., 2015) highlighted the possibility that cultural differences could lay at the semantic level. Moreover, it is likely that participants belonging to the Singaporean sample, representing a collectivist population, could express preoccupation towards other people's opinions compared to the Italian group, displaying greater levels of anxiety and avoidance (Hao et al., 2019). However, due to the paucity of references regarding this point, results need to be interpreted cautiously. Additionally, we included in our analyses the effect of allelic variation of one *OXTR* gene SNP, namely rs53576. We were expecting to find effects for the interaction between the genetic and perceived caregiving variables, with different influences in the groups (tested in *HP1* and *HP2*). Moreover, we explored a more intertwined model, adding the influence of the cultural environment (tested in *HP3*).

2.4.1 Gene-By-Environment Interaction within the Western-Oriented Sample and the Eastern-Oriented Sample Evaluated Independently

With regards to the Italian sample, the first step considered only the *OXTR* variation in explaining the levels of anxiety and avoidance. Perceived maternal features were progressively entered into the model, both resulting as strong predictors for anxiety, with care displaying a negative association and overprotection a positive one. In the subsequent steps, recalled paternal characteristics were added to the model, and the care dimension for the father resulted as a predictor for anxiety as well. This might reflect the diversified, but equally important, contributions that both parents produce in their offspring, leading to different outcomes as a consequence (Rork and Morris, 2009). In the model of interaction tested at the last stage, recalled maternal overprotection appeared to explain levels of anxiety, with a positive correlation: the greater the overprotection felt, the higher the levels of experienced anxiety. Here, Italian individuals with a past of perceived maternal overprotection reported higher levels of anxiety than those who recalled a less controlling relationship with their mothers. Perceived maternal control during childhood, assessed in terms of overprotection, seemed to be the construct that better explained the level of anxiety in adult relationships. This result was in line with the theoretical framework of the development of attachment (Bowlby, 1988), and furthermore, it was also supported by other studies (Parker and Lipscombe, 1981; Rork and Morris, 2009; Raudino et al., 2013; Kiel and Kalomiris, 2019; Smout et al., 2020). The results sug-

gested that both parents, to different extents, contributed in explaining the formation of anxiety-related patterns in adult social behavior. With regards to the experienced avoidance in adulthood, we found that maternal care contributed to the unique variance as a predictor, negatively associated. Although no other variables alone were proven robust predictors, the interaction between the genotype and early parental bonding dimensions substantially increased the explained variance in adult avoidance. However, due to the choice of a highly conservative correction method, the effect of maternal care emerging from the interactive model tested on avoidance did not reach the significance level. Interestingly, in the Italian sample, features of the mother appeared to influence the formation of psychological constructs of close relationships more than those of the father, highlighting the importance of the specific parental role in explaining outcomes in adult relationships (Land et al., 2011; Gallagher and Cartwright-Hatton, 2008). Moreover, within the final stages of the HMR, no significant effect was found for the interaction between *OXTR* rs53576 and the parental bonding dimension on anxiety or avoidance, not confirming the first hypothesis. Overall, these results suggest that the quality of familiar bonds in this population, where higher levels of expressed emotions often characterize the relationship between parents and offspring (Pellerone et al., 2017; Pace et al., 2016; Laudani et al., 2014), could affect the experience of close relationships in adulthood more independently of the genetic sensitivity, invalidating the starting *HP1*.
Concerning the Singaporean sample, the development of HMRs on this population overall revealed distinct patterns of parental boding and genotype on adult attachment as a potential effect of Eastern cultures. As for adult anxiety, recalled paternal care and overprotection contributed more significantly to the model when respectively entered. Although the interaction between genotype and parental features did not improve the model in terms of the total amount of variance, an interaction effect between genotype and maternal overprotection emerged at this final stage. Such an effect was marginally significant, thus did not persist when the

correction was applied.

Unlike the Italian sample, neither genotype, nor the recalled parental features resulted as a significant predictor of adult avoidance across the different steps of the model whose variance remained stable. In the final step, where all the targeted variables were included, maternal care was the strongest predictor of avoidance in adult close relationships with a negative trend. Moreover, the interaction between *OXTR* variations and maternal care reached statistical significance as well. In particular, the two variations followed a mutually opposite pattern of association, displaying a slight positive correlation for maternal care over avoidance levels for G-carriers and a negative one for A/A homozygotes. In line with *HP2*, the present cross-interaction supported the assumption of a differential sensitivity to environmental influences among carriers of distinctive genetic phenotype in *OXTR* rs53576 (Ebstein et al., 2012, 2009; Belsky and Pluess, 2009a). While evidence suggested overall effects of *OXTR* rs53576 on prosocial mechanisms, such as empathy or seeking emotional support, outcomes on attachment style were not consistent. Our results may reflect that the boundary condition plays a stronger role when it comes to adult attachment dimensions (Gong et al., 2020; Li et al., 2015; Rodrigues et al., 2009); thus, caution is needed in addressing the A/A variant as a risk factor for non-optimal patterns of attachment. Currently, there are few studies examining the effects of the interaction of recalled parental bonding and *OXTR* rs53576 on adult attachment dimensions in Eastern populations, considering the ethnic group separately (Li et al., 2015; Rodrigues et al., 2009; Gillath et al., 2008), advocating the need for a focus on the importance of biological differences and distinct allelic distributions.

We observed that the effects in the two groups differed, especially in the relationship between recalled maternal bonding and the attachment dimension in adult relationships, reflecting the typical traits of familiar bonds: with regards to the Italian sample, where great attention is projected on the child and levels of emotions expressed are high (Laudani et al., 2014), the construct of overprotection was associated with anxiety in adult relationships. According to the traits depicting individualistic cultures, the person is expected to be self-reliant and not to depend on other people for support, which in turn might be reflected in greater anxiety expressed or experienced, instead of avoidance (Sümer and Yetkili, 2018). On the other hand, in the Singaporean sample, where interdependence represents a typical trait in social groups, starting from the family, the avoidant pattern of behavior can describe a greater form of distress in relationships, compared to Western-oriented groups (Sümer and Yetkili, 2018; Friedman et al., 2010).

2.4.2 Gene-By-Culture Interactions in the Total Sample

While the gene-by-environment framework focuses predominantly on external factors that characterize individual experience, the gene–culture interaction field of research focuses on the socio-cultural context. Within this theoretical frame, variants conferring genetic susceptibility can amplify typical cultural tendencies (Kim et al., 2010), such as interdependence (Luo et al., 2015). Adopting HMRs, we aimed to explore the influence of the cultural environment and of its interaction with genetic variations sensitive to external context, such as perceived parental caregiving.

In reference to the HMRs developed on adult anxiety, culture was the first variable added to the model, explaining a significant portion of variance. The subsequent addition of genotype did not increase the variation in anxiety, but this increase was true for the addition of maternal and paternal care, as well as paternal overprotection at different steps, respectively. Finally, the interaction among the culture, genotype, and parental bonding dimensions maximized the variance on adult anxiety. Despite this achievement, the model of interaction did no not reveal consistent effects on adult anxiety.

In the context of the HMRs advanced for adult avoidance, culture still was a key variable that was able to increase the variance significantly. Discordant with the significant effects of the numerous parental features on the variation in anxiety, only maternal care enlarged the amount of explained variation in avoidance. In accordance with the final model observed from the HMRs on anxiety, the highest quantity of total variance was reached when the interaction among the culture, genotype, and parental bonding dimensions was verified on avoidance.

From the model of the three-way interaction, multiple effects were observed. Firstly, maternal overprotection positively predicted adult avoidance when the cultural and genotype influences were not further examined. Secondly, the cultural component played a dominant role over experienced avoidance in adult close relationships. We observed that the effects on the two groups were different, especially in the relationship between culture and maternal overprotection. Specifically, maternal overprotection was positively associated with adult avoidance for both Western and Eastern samples. However, the Western-oriented participants reported lower mean levels of avoidance from the partner than the Eastern-oriented individuals. Mousavi and colleagues, although framing their exploration in a wider perception of anxiety, including social phobia, which is related to avoidant patterns of behavior, provided evidence that the perception of parental control or overprotection was reported in a stronger extent in a Caucasian sample (Mousavi et al., 2016). Thirdly, the contributing action of the genetic predisposition driven by *OXTR* rs53576 was also identified. In this regard, the significant interaction between genotype and maternal overprotection predicted adult avoidance when the participants were conceived together and independently from the cultural belonging to the group. However, the proper interpretation of this effect faced several difficulties in light of the different alleles' frequency between Western and Eastern samples.

Analyses referring to the gene-by-culture frameworks displayed an interesting result: the different levels of associations between the genetic carriers A/A, A/G, and G/G and maternal overprotection on the adult avoidance for the Western-oriented and Eastern-oriented sample disclosed peculiar attachment patterns as a function of a differential genetic susceptibility to the external environment (Kim et al., 2011a, 2010). Here, the less common variation (A/A for the Italian sample, G/G for the Singaporean group) was the one more directly correlated to greater levels of avoidance for higher levels of perceived maternal overprotection. Similar results were found by Kim and colleagues when exploring the role of the culture using a gene-by-environment approach between individualistic (American) and collectivist (Korean) populations in investigating emotion suppression (Kim et al., 2011a). Avoidance, likewise emotion suppression, can be described as a coping strategy to deal with stressful experiences (Kashdan et al., 2006). Analogous to the findings of Kim and colleagues, greater levels of avoidance were observed among G/G-carriers in the Singaporean sample, compared to those carrying two copies of the A variant. Conversely, in the Italian group, G/G-carriers showed significantly lower levels of avoidance compared to the A/A-carriers. These findings suggested that the allelic variation retained to confer greater sensitivity to environmental input was correlated with more optimal outcomes involving social and emotional strategies, according to the specific societal context (Kim et al., 2010, 2011a). Interestingly, in the Singaporean sample, people carrying the A/G variation displayed an opposite trend in terms of negative relationships with avoidance compared to both the positive associations of A/A- and G/G-carriers with the same ECR-R dimension. In the literature, evidence reports results for the heterozygous variation together with the less common homozygous pair of alleles in order to correct skewed distributions (Kim et al., 2011a); hence, this outcome requires caution when it comes to interpretation. Unexpectedly, the trend of avoidance scores in the Singaporean sample decreased for A/G-carriers, but increased for A/A and G/G homozygotes, suggesting a broad variability in perceived maternal control over close adult relationships.

Chapter 3

How does early caregiving interact with genetic factors in moderating online social attitudes?

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[0] Chapter based on a preregistered and published study:

Study 2. Bonassi, A., Cataldo, I., Gabrieli, G., Foo, J. N., Lepri, B., Esposito, G. (2020). Oxytocin receptor gene polymorphisms and early parental bonding interact in shaping Instagram social behavior. *International journal of environmental research and public health*, 17(19), 7232. DOI: 10.3390/ijerph17197232.

The research presented in this chapter is linked to the following unpublished study (preprint) of the research project:

Study D. Bonassi, A., Cataldo, I., Gabrieli, G., Tandiono, M., Foo, J. N., Lepri, B., Esposito, G. (2020). The interaction between serotonin transporter allelic variation and maternal care modulates sociability on Instagram. *PsyArXiv*. DOI: 10.31234/osf.io/dkvnf.

3.1 Introduction

From the first years of life, infants are exposed to a stimulating environment that strengthens their social bonds with parents and family members (Seifer and Schiller, 1995). During infancy and childhood, the individual lays the basis for a complex pattern of exchange and engagement through his/her interaction with relatives and peers (Fagot, 1997). As explained in the previous chapters, the distinctive pattern in early attachment with caregivers can be stable across human development and influence adult attachment with partners (Feeney, 1996; Griffin and Bartholomew, 1994). Within the interaction between caregivers and offspring (Esposito et al., 2013), high quality parental bonding enhances children's self-efficacy (Meins, 2013), as well as social and emotional communication (Markiewicz et al., 2001), while reducing psychological (Diamond and Hicks, 2004) and physiological (Schoenmaker et al., 2015; Robles and Kane, 2014) stress. Parental bonding represents the core causal factor of the main developmental stages, which remain open to modulation due to experience and exposure to further environmental events (Waters et al., 2000).

Currently, both digital and physical spaces can forge social bonds and become the theaters of online and offline interactions that affect relationships among people. The adoption of technological devices allows children to explore social media platforms and online worlds (Hutchby and Moran-Ellis, 2013). Hence, the growing social skills in virtual and real environments shape adolescents' (Espinoza and Juvonen, 2011; Vagos, 2009; Blakemore, 2008) and adults' online and offline behaviors (Rook, 1984; Lenhart et al., 2010; Lin et al., 2016). In particular, the ubiquitous usage of Social Network Sites (SNSs) has created a virtual environment where social interactions can happen anytime and anywhere (Smock et al., 2011; Chen, 2011; Hu et al., 2014; Archambault and Grudin, 2012; Van Dijck, 2013). Among the different platforms, Instagram, one of the most popular sites for youths (Greenwood et al., 2016), focuses on photo-sharing and visual content. It is mainly characterized by various online social behaviors such as scrolling through followings' contents, watching stories, publishing posts, tagging followers, commenting on photos, and chatting privately (Ferrara et al., 2014).

With the advent of Instagram, kids are early participants of social media. Parents become prey to "sharenting", the phenomenon that describes the tendency to exhibit pictures of their children online (Choi and Lewallen, 2018). Interestingly, recent findings have highlighted a disagreement regarding the positive and negative outcomes of online social interactions on SNSs. For instance, the frequency of Facebook and Instagram usage, as well as high rates in reported self-attractiveness (Antheunis and Schouten, 2011) are associated not only with a higher self-esteem (Valkenburg et al., 2006), but also with depressive symptoms (Rosenquist et al., 2011). Furthermore, Instagram improves happiness and decreases solitude with the intimacy offered by the images (Pittman and Reich, 2016). At the same time, an increased number of Instagram posting activities, combined with individual body dissatisfaction, increases the probability of engaging in negative romantic relationships (Ridgway and Clayton, 2016). The reason for Instagram use was also traced to a high need for interpersonal interaction and dominant traits in narcissism (Sheldon and Bryant, 2016; Lee et al., 2015). The same parents share their "family snapshots" to prove that the "merry family ideal" and the "cute child ideal" have come true (Le Moignan et al., 2017). Although several papers investigated how parental factors are associated with user activity on Facebook (Kross et al., 2013; Junco, 2012b,a) and Instagram (Le Moignan et al., 2017; Thimm and Nehls, 2017; Choi and Lewallen, 2018), there is a lack of research focused on the interplay between Instagram activity and early attachment with parents. This gap is even more evident if the potential relationship between attachment and genetic factors is considered. Only a few studies recently probed the genetic influence on the frequency of social media use (York, 2017; Bonassi et al., 2020c). The evolutionary tendency to be social can be modulated by genetic factors, which, in turn, are regulated by the environmental actions across the human lifespan, thus conferring nuanced levels of sensitivity to the experiences. Based on the model of the plasticity of genes (Belsky et al., 2009; Belsky and Pluess, 2009b), it is not only the protective factor versus the risk factor of genes that determines human behavior. Indeed, one must also take into consideration the quality of environmental factors that interact with allelic expression in shaping physiological responses and then behavioral patterns that foster environmental adaptation (Boyce and Ellis, 2005).

According to the Susceptibility Hypothesis (Belsky et al., 2015), alleles (i.e., G or A) of a given genetic region (i.e., *OXTR* rs2254298) are associated with different degrees of sensitivity to the environmental effects (i.e., quality of early parental care) (Esposito et al., 2017c). Here, a genetic risk factor makes the individual genetically sensitive or susceptible to life events and individual experience (Ellis et al., 2011; Truzzi et al., 2018).

In the context of sociability, people with high genetic sensitivity will exhibit a more adaptive social behavior when exposed to a positive environment (i.e., a warm relationship with parents) (Pluess and Belsky, 2013; Cataldo et al., 2021a). However, they will display less adaptive social behavior if they go through negative events (i.e., the loss of a parent, child abuse, or maltreatment) (Belsky et al., 1991; Belsky, 1993). Conversely, low genetic sensitivity and vulnerability will make someone more resistant to the effects of early traumatic episodes (i.e., parental separation or abandonment), as well as beneficial events (i.e., competent caregiving), generating a decreased social response (Pluess and Belsky, 2010).

Within this debate, multiple studies have attributed a key role in the biological explanation of social behavior to the hormone oxytocin (Bartz et al., 2011; Feldman et al., 2016). Specifically, rs53576 and rs2254298 polymorphisms, encoded by the*OXTR*, correlate with social behaviors, social cognition, and empathy (Ebstein et al., 2012; Wu et al., 2012). For each region, two allelic structures have been observed to play a role as determinants in social development: guanine (G) to adenine (A) substitution shows greater sensitivity to the environment and influences responses to stressful life events (Cataldo et al., 2018b). However, from the previous results, it is not possible to unequivocally establish which variation—G or A—is more associated with less adaptive social responses.

Concerning rs2254298, a history of paternal overprotection was found to moderate the heart rate responses to socially distressing stimuli (increased for A-carriers, but decreased for G/G homozygotes) (Esposito et al., 2017d). A-carriers also showed lower empathetic levels than G-carriers regardless of parental warmth (Wu et al., 2012).

As for rs53576, individuals with the G variation show a variety of favorable features when compared to A-carriers, such as higher levels of trust (Krueger et al., 2012), dispositional empathy (Smith et al., 2014), greater sympathetic response to stressors (Truzzi et al., 2018), and more sensitivity to social cues (Rodrigues et al., 2009) and social interactions (Li et al., 2015). Moreover, social support before a distressing task was observed to reduce cortisol response in G-carriers, but not in A/A homozygotes (Chen et al., 2011b).

Taken together, these scientific contributions point out that genetic expression, combined with early environmental exposure, contribute to the shaping of adult sociability. However, the role played by specific genetic predispositions (i.e., the ones related to early environment exposure during infant-parent interaction) on the online social relationships of adults is considerably underexplored.

This study investigates how *OXTR* and caregivers' propensities during childhood interact in modulating adult online relationships on Instagram. Specifically, two *OXTR* Single-Nucleotide Polymorphisms (*OXTR* SNPs: rs2254298 and rs53576) for the genetic component and the Parental Bonding Instrument as the assessment for the parent-child recalled bonding were considered. Likewise, the Instagram number of (i) followed users (here called "followings"), (ii) published posts, (iii) followers, and (iv) a further combined index, called the “Social Desirability Index” (SDI), were selected as the main social media variables.

This goal was addressed with the formulation of a combined directional hypothesis to evaluate both correlations and mean level similarities and differences between conditions. In favor of the Susceptibility Hypothesis, for each Instagram variable, an interaction effect between the genetic component and the parental attachment scores, independent of gender, was hypothesized. More specifically, adult Instagram users with a genetic risk factor (*OXTR* rs2254298 A-carriers, *OXTR* rs53576 G-carriers) and who were exposed to a beneficial and positive early relationship with their parents (high parental care, low parental overprotection) would show increased online social activity (higher number of posts and followings) compared to less vulnerable genetic carriers (*OXTR* rs2254298 G/G homozygotes, *OXTR* rs53576 A/A homozygotes). Conversely, Instagram users with a genetic risk factor and who were exposed to an adverse and negative early relationship with parents (low parental care, high parental overprotection) would show decreased online social activity as described by a lower number of posts and followings compared to less vulnerable genetic carriers.

3.2 Material and Methods

3.2.1 Participants

Sixty-one (N = 61) non-parent Singaporean adults were recruited among the students of the Nanyang Technological University. Exclusion criteria were: (i) current or lifetime history of genetic, neurological, or psychiatric disorders, (ii) age higher than 30 years old, and (iii) being a parent. Inclusion criteria were: (i) owning an Instagram account; (ii) using Instagram at least once a week. Four participants were not included due to technical issues; thus, the final sample consisted of 57 Singaporean adults (16 males and 41 females) aged 18–25 years old (M = 20.82, SD = 1.59).

3.2.2 Procedure

Participants were recruited among students of the Nanyang Technological University and rewarded with academic credits for their participation. Prior to data collection, participants signed an informed consent form and provided demographic information. Then, using the web-based survey platform Qualtrics, participants filled in a self-reported questionnaire (i.e., the Parental Bonding Instrument) to assess their recalled parental bonding during childhood. In addition, a sample of buccal mucosa was collected from each participant by using sterile cotton swabs[1] and sent to a laboratory for genotyping. Lastly, participants provided the link to their Instagram profile, and using a Python program, four indicators of their Instagram activity were automatically extracted. Where the Python program failed in extracting the data, Instagram information was collected manually. The four indicators of Instagram activity, later elaborated, were publicly available regardless of the privacy settings of each user's account. This research was approved by the Ethical Committee of Nanyang Technological University (IRB-2015-08-020-01) and preregistered on the Open Science Framework[2]. The final dataset generated for this work is available online on the Data Repository of the Nanyang Technological University (DR-NTU Data) Bonassi et al. (2019).

3.2.3 Parental Bonding

The Parental Bonding Instrument (PBI) (Parker et al., 1979) is a 50 item self-reported questionnaire widely adopted to measure individual self-perception of attachment with their parents during the age of 0–16. In this questionnaire, participants reported the quality of the parental bonding, as well as the caregiving behavior they experienced during childhood and adolescence on a Likert scale from 0 ("very unlike") to 3 ("very like"). The PBI (average Cronbach's $\alpha = 0.88$) investigates two main dimensions of recalled care and overprotection of both parents, calculated

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[1] Medline MDS202010Z Sterile Cotton Tipped Applicator, 6"

[2] The public registration of this study can be found on the Open Science Framework at the following address: https://osf.io/j9nqc.

by summing the items and considering the scores of six specific items as reversed for each dimension (Table 3.1). The questionnaire is then divided into four subscales: paternal care (12 items), maternal care (12 items), paternal overprotection (13 items), and maternal overprotection (13 items). Parental care (e.g., "Appeared to understand my problems and worries") is a measure of affection, warmth, emotional affinity, and empathy, and its scoring is positively correlated with the quality of the parental bonding (Dalsant et al., 2015): the higher the score, the higher the level of affection perceived during the past early parent-child interactions. On the other hand, parental overprotection (e.g., "Tried to control everything I did") is a measure of the level of control, intrusion, and restriction from autonomy, and its scoring is negatively correlated with the quality of the parental bonding (Carter et al., 2001): the higher the score, the higher the level of oppression perceived during the past early parent-child interactions.

PBI Subscale	**Lower α**	**Raw α**	**Upper α**
Paternal care	0.83	0.88	0.93
Maternal care	0.88	0.91	0.95
Paternal Overprotection	0.79	0.85	0.91
Maternal Overprotection	0.84	0.89	0.93

Table 3.1: Summary of Cronbach's α for each subscale of the Parental Bonding Instrument.

3.2.4 Genetic Assessment

The same data extraction procedure used by Bonassi et al. (2017) was adopted in this study. Specifically, DNA derivation and genotyping were executed by ACGT, Inc. (Wheeling, IL, USA). DNA was extracted from each kit using the Oragene DNA purifying reagent, and DNA concentrations were assessed through spectroscopy (NanoDrop Technologies, Wilmington, North Carolina, USA). Each DNA sample was magnified through Polymerase Chain Reaction (PCR) for the *OXTR* gene rs2254298 region target with the primers 5-TGA AAG CAG AGG TTG TGT GGA CAG G-3 and 5-AAC GCC CAC CCC AGT TTC TTC-3.

A PCR reaction of 20 ll comprising 1.5 ll of genomic DNA from the test sample, PCR buffer, 1 mM each of the forward and reverse primers, 10 mM deoxyribonucleotides, KapaTaq polymerase, and 50 mM MgCl2 was conducted. The PCR process consisted first of a 15 min denaturation at 95 °C, 35 cycles at 94 °C (30 s), 60 °C (60 s), and 72 °C (60 s), and a final 10 min protraction at 72 °C. PCR reactions were genotyped with an ABI 3730xl Genetic Analyzer[3] and standardized with GeneScan 600 LIZ[4] size standards on each sample. Genotypic data were examined using GeneMapper ID[5].

For this DNA region, participants having at least one A allele (A/A homozygotes or G/A) were classified into a single A-carriers group. The average distribution of the different genotypes in the Asiatic population is 61% for G/G homozygotes and 39% for A-carriers [6], whereas the distribution in this sample was 58% for G/G homozygous and 42% for A-carriers. Genotype frequencies were as follows: A/A = 4 (7.02%), G/A = 20 (35.09%), G/G = 33 (57.90%).

This genotype distribution follows the Hardy–Weinberg equilibrium (X^2 (1) = 0.16, ns). Participants' age ($t(55) = 0.64$, $p = 0.53$) and gender ($X^2(1) = 0.55$, $p = 0.46$) did not significantly differ between the two groups G/G versus A.

Similar DNA procedures were applied to the *OXTR* gene rs53576 region target. However, the forward and reverse primers that were considered were instead 5-GCC CAC CAT GCT CTC CAC ATC-3 and 5-GCT GGA CTC AGG AGG AAT AGG GAC-3. For this DNA region, study participants having at least one G allele (G/G homozygotes or A/G) were classified into a single G-carriers group. The average distribution of the different genotypes in the Asiatic population is 30% for A/A homozygotes

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[3] Applied Biosystems Inc., Zug, canton of Zug, Switzerland

[4] Applied Biosystems, Inc.

[5] Applied Biosystems, Inc.

[6] 1000 Genomes project, BioSamples: SAMN07486027-SAMN07486024, dbSNP (Short Genetic Variations), 2017

and 70% for G-carriers[7], whereas the distribution in this sample was 35% for A/A homozygous and 65% for G-carriers. In detail, genotype frequencies were as follows: A/A = 20 (35.09%), A/G = 32 (56.14%), G/G = 5 (8.77%). This genotype distribution follows the Hardy–Weinberg equilibrium (X^2 (1) = 2.43, ns). Participants' age ($t(55) = 0.09$, $p = 0.93$) and gender ($X^2(1) = 0.55$, $p = 0.46$) did not significantly differ between the two groups A/A versus G.

3.2.5 Instagram Variables

Four variables (i.e., number of followings, number of posts, number of followers, and the Social Desirability Index) were extracted from each participant's Instagram profile. In the subsequent paragraphs, these variables are described in detail.

Number of Followings

The number of followings is the number of followed profiles by a given participant. It describes the unidirectional extension of the social network from a given individual to other Instagram users. Participants with higher following numbers tend to invest more time in virtual social behaviors than the ones with few contacts (Sherlock and Wagstaff, 2018). Indeed, following more people means managing more social interactions (Araújo et al., 2014), being exposed to more content, and consuming more activity in searching for other users or remaining updated with other users' news (Jang et al., 2015). This is particularly relevant if it is considered that Instagram users tend to compare themselves with others. People judge the way that the users who they follow behave or appear. This causative chain induces Instagram users to evaluate their own real-life and regulate their virtual activity by comparing it to the ones in their network.

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[7] 1000 Genomes project, BioSamples: SAMN07486027-SAMN07486024, dbSNP (Short Genetic Variations), 2017

Number of Posts

The number of posts reflects the individual tendency to publish and share content and information on the personal profile. Differently from other SNSs, Instagram posts can only consist of pictures, and a brief caption of the pictures is optional. Previous research has shown that the number of posts is also positively associated with the users' depressed mood (Frison and Eggermont, 2017) and the users' body image (Chang et al., 2019). Thus, these studies reported that intense online activity (i.e., publishing content) could be a marker of psychological vulnerability (Lup et al., 2015; Chancellor et al., 2016; Holland and Tiggemann, 2017; Barry et al., 2019). Moreover, the number of posts also describes: (a) the Instagram user not only as an observer, but also as a proactive and constructive agent of the social network, (b) the user's availability to expose himself/herself to the others' judgment for different personal reasons (e.g., openness, appearance, egocentricity, need for approval) and, at the same time, his/her aim at influencing others' behavior (Sannon et al., 2019), and finally, (c) the need to be pro-social and to connect with others by engaging with them through posts.

Number of Followers

The number of followers underlines the multi-directional extension of the social network from other users to the assessed study participant. From a cognitive-behavioral view, followers' approval operates as a positive or negative reinforcer of the user's online behavior and as a moderator of the user's social cognition. Therefore, the social network dictates the laws of online behavior, imposing and raising the ideal standard of virtual social interactions to which each single user should conform to increase his/her likeability (Cheung, 2014). The number of followers could be affected by the privacy level set by the user for his/her profile. Indeed, users with a private profile could get less followers than users with a public profile since a private profile can be followed only upon permission of the owner.

Social Desirability Index

The Social Desirability Index is defined as the ratio between the number of followers and the number of followings, and it was estimated in order to investigate the asymmetry between these two quantities for each study participant's network (Agam, 2017). Interestingly, this ratio can disclose the tendency of some Instagram users to maximize the number of followers at the expense of the number of followings (Erz et al., 2018).

3.2.6 Statistical Analysis

The statistical analysis was conducted with R (Version 4.0.0). Each Instagram variable was standardized using z-scores (see Table 3.2).

Variables	**Min**	**1st Q**	**Median**	**Mean**	**3rd Q**	**Max**
Followings Number	−1.54	−0.77	−0.12	−0.12	0.52	1.80
Posts Number	0.33	0.39	0.49	0.56	0.67	1.19
Followers Number	−0.80	−0.50	−0.16	−0.11	0.22	1.45
Social Desirability Index	−1.16	−0.28	−0.13	−0.16	−0.03	0.61
Maternal care	0.00	4.00	8.00	9.97	14.00	28.00
Paternal care	0.00	9.00	14.00	14.49	18.00	30.00
Maternal overprotection	8.00	18.00	23.00	23.82	30.00	37.00
Paternal overprotection	11.00	23.00	29.00	27.05	32.00	37.00

Table 3.2: Summary of the descriptive statistics for each continuous variable. The distribution of each variable is described in terms of the Minimum (Min), first Quartile (1st Q), median, mean, third Quartile (3rd Q), and Maximum values (Max).

Univariate and multivariate distributions of Instagram variables and attachment scores were examined for normality and the presence of outliers (Ben-Gal, 2005). The distance of each observation to the centroid was estimated for outliers defined as having a value equal to 2 *SDs* above/below the mean. Out of the total of 57 observations for each Instagram variable, three extreme values were considered outliers for the number of followings and for the number of posts, two values for the SDI, and one value for the number of followers. Outliers were treated by means of winsorization (Kwak and Kim, 2017), a method for treating outliers based on the weight modification of the extreme values. Thus, for each Instagram variable, this approach allowed the replacement of the outliers with the mean value in observations, obtained by excluding the outliers.

Then, for each Instagram variable, density and quantile-quantile plots were visualized, and the related skewness and kurtosis were computed (see Table 3.3). The obtained results were considered acceptable to prove a normal univariate distribution (Gravetter and Wallnau, 2005). As for the number of posts, whose sampling did not show a Gaussian distribution, a logarithmic transformation was applied to assure the applicability of statistical parametric tests (see Table 3.3).

Variables	**Skewness**	**Kurtosis**
Followings Number	0.29	−0.72
Posts Number	1.69	2.56
Log-transformed Posts Number	1.22	0.82
Followers Number	0.79	0.17
Social Desirability Index	−0.70	2.63

Table 3.3: Summary of skewness and kurtosis values for each Instagram variable. The log-transformed number of posts shows an enhancement of the power values compared to the same non-adjusted variable.

Additionally, the assumption of the homogeneity of variance and multicollinearity across the sample was ascertained.

A preliminary analysis of Instagram variables was conducted to exclude any effect that could be attributable to a difference in the distribution of participants' gender (4 repeated measures, corrected $\alpha = 0.0125$).

Although hypothesis-driven analysis was fixed to the number of Instagram followings and posts, the analogous statistical procedure was adopted for exploratory analyses conducted on the number of Instagram followers and the SDI. Next, a differential Bonferroni correction was applied for the hypothesis-driven tests (2 repeated measures for each genetic variable, corrected $\alpha = 0.025$) and the exploratory tests (2 repeated measures for each genetic variable, corrected $\alpha = 0.025$). Throughout the data analysis, the genetic variables, *OXTR* rs2254298 and *OXTR* rs53576, were used as single predictors in separate analyses.

For each Instagram variable, one multiple regression was performed with the Instagram value as the dependent variable, the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as a between-subjects factor, and all the

PBI dimensions (i.e., maternal care, maternal overprotection, paternal care, and paternal overprotection) as continuous predictors. To appropriately test the hypotheses, for each Instagram variable, one linear regression was also performed with the *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subjects factor, with the other parameters fixed and unvaried. For the overall Instagram-dependent variables, two main effects and two 2 way interaction effects related to *OXTR* rs2254298 were considered and represented by bar plots and scatterplots with linear models. Given that this study is focused on the role played by genetics in regulating Instagram social behavior, only the main effects of genotype and any significant interactions of a PBI dimension with genotype are discussed. The main effects of the PBI dimensions (i.e., those shown below) were included in the model only to support the plausible interpretation of data according to the gene*environment perspective. Pearson's r and Fisher's z (Diedenhofen and Musch, 2015) coefficients were also assessed to further investigate the effect of the continuous predictors on the dependent variable.

For each significant interaction effect between the PBI covariate and the genotype on the Instagram-dependent variable, the sample was divided into two groups (low vs. high PBI dimension) by the median split procedure. Post-hoc Student's t-tests were computed within the low vs. high PBI groups to examine hypothetical significant differences between the two genetic carriers on Instagram behavior.

R squared and Cohen's d were estimated to evaluate the magnitude of the significant effects for linear models and Student's t-tests, respectively. Post-hoc statistical power for linear multiple regression (fixed model, R^2 deviation from zero) (Faul et al., 2009) calculated with G*Power software (Version 3.1) is reported for each statistical test.

3.3 Results

3.3.1 Instagram Variables: Preliminary Results

Four preliminary two tailed Student's t-tests were made to be sure that any significant effect on Instagram variables could not be attributed to participants' gender (corrected $\alpha = 0.0125$). As expected, no significant differences in the standardized Instagram number of posts, followers, and the standardized SDI were found between male and female participants (Table 3.4). However, contrary to the expectations, the number of Instagram followings was higher in males than females ($t = 2.60$, df $= 55$, $p < 0.012$) (Figure 4). As a result, participant gender was included as a between-subjects variable on the number of Instagram followings.

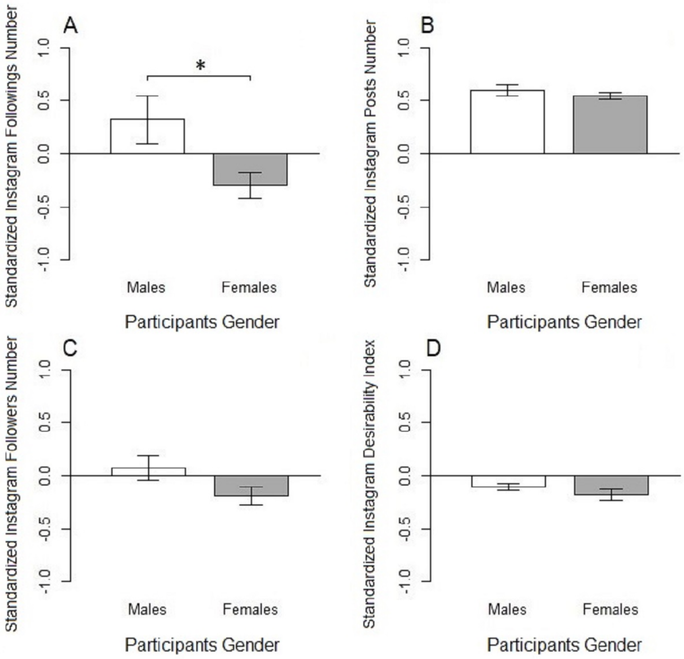

Figure 4: Effect of participants' gender on each standardized Instagram variable. Bar plots are reported according the following order: (**A**) number of followings; (**B**) number of posts; (**C**) number of followers; (**D**) Social Desirability Index (* $p < 0.0125$).

Instagram Variables	**Males**	**Females**
Followings Number	0.32 (0.23)	−0.28 (0.12)
Posts Number	0.60 (0.05)	0.55 (0.03)
Followers Number	0.08 (0.12)	−0.19 (0.08)
Social Desirability Index	−0.11 (0.03)	−0.18 (0.05)

Table 3.4: Mean values in male and female participants on the overall Instagram variables. Standard Error Means (SEM) are reported between parentheses.

3.3.2 Instagram Effects: ***OXTR*** rs2254298

Number of Instagram Posts

The results of the regression analysis on the standardized number of Instagram posts indicated that paternal care was a significant covariate in both the main and the interaction effect with genotype (R^2 (95% CI [0.06, 0.47]) = 0.31, power = 0.95). Although a main effect of paternal care was found for the number of Instagram posts ($\beta = 0.02$, SE = 0.01, $t = 3.12$, $p = 0.003$), the post-hoc two tailed Student's t test revealed that the number of Instagram posts was not significantly different between the low vs. high paternal care groups ($t = -0.71$, df = 55, ns) (see Table 3.5). A significant interaction between paternal care and genotype also emerged for the number of Instagram posts ($\beta = -0.03$, SE = 0.01, $t = -3.60$, $p = 0.0008$). The distribution of genotypes, GG vs. A-carriers was not significantly different between high vs. low paternal care (X^2 (1) = 0.61, ns). No main effect of genotype or other interactions with genotype were significant. Paternal care was positively associated with the number of Instagram posts for A-carriers ($t(24) = 4.27$, df = 22, $r = 0.67$, $p < 0.0003$), but negatively associated with the number of Instagram posts for G/G homozygotes ($t(33) = -1.42$, df = 31, $r = -0.25$, ns) (see Figure 5). Although only one Pearson's r was significant, the difference between the slopes for G/G and A-carriers, calculated with Fisher's z, was statistically significant ($z = 3.76$, $p = 0.0002$). As predicted, the one tailed post-hoc Student's t tests on the A-carriers vs. G/G in the low and high paternal care groups (corrected $\alpha = 0.025$) revealed that the number of

Instagram posts was significantly different between A-carriers and G/G homozygotes only when they reported past experiences of low paternal care ($t = -2.35$, df $= 29$, $p = 0.013$, $d = 0.85$), but not when they had past experiences of high paternal care ($t = 1.91$, df $= 24$, $p = 0.034$, $d = 0.79$) (see Table 3.5 and Figure 5). The homogeneity of variance of the number of Instagram posts by paternal care was verified ($K^2(1) = 0.49$, ns).

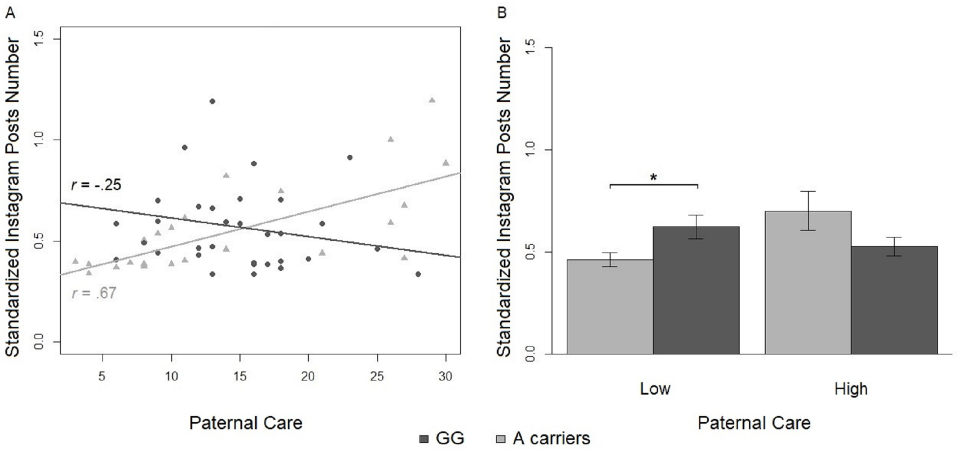

Figure 5: (**A**) Effect of the interaction between paternal care and genotype on the standardized number of Instagram posts. Correlations between the number of Instagram posts and the reported paternal care. Black circles = G/G homozygotes; grey triangles = A-carriers. Lines constitute the linear models for G/G homozygotes (black) and A-carriers (grey). *r*-values refer to Pearson's r correlations. (**B**) Comparison between the number of Instagram posts in G/G homozygotes (black) and A-carriers (grey) divided into high and low paternal care (* $p < 0.025$).

Instagram Variables	**Low**	**High**		
Posts Number	0.54 (0.04)	0.59 (0.05)		
Social Desirability Index	−0.14 (0.06)	−0.18 (0.05)		
Instagram Variables	**Low/A**	**Low/GG**	**High/A**	**High/GG**
Posts Number	0.46 (0.03)	0.62 (0.06)	0.70 (0.10)	0.52 (0.05)
Social Desirability Index	−0.04 (0.08)	−0.25 (0.10)	−0.29 (0.06)	−0.13 (0.06)

Table 3.5: Top section: mean values of variables with main effects. Line 1: mean values in low and high paternal care on the number of posts. Line 2: mean values in low and high maternal overprotection on the Social Desirability Index. Bottom section: mean values of significant interactions. Line 1: mean values in A-carriers and G/G homozygotes divided into low and high paternal care on the number of posts. Line 2: mean values in A-carriers and G/G homozygotes divided into low and high maternal overprotection on the Social Desirability Index. Standard Error Means (SEM) are reported between parentheses.

Social Desirability Index

The results of the multiple regression on the standardized SDI reported a significant main effect of maternal overprotection and a significant interaction between the same covariate and the genotype (R^2 (95% CI [0.00, 0.36]) = 0.22, power = 0.77). Although not the main focus of the paper, a main effect of maternal overprotection was found for the SDI ($\beta = -0.03$, SE = 0.01, $t = -2.58$, $p = 0.013$). However, post-hoc two tailed Student's t-test revealed that the SDI was not significantly different between the low and high maternal overprotection groups ($t = 0.50$, df = 55, ns) (see Table 3.5).

From exploratory analyses, a significant interaction between maternal overprotection and genotype emerged for the Instagram SDI ($\beta = 0.04$, SE = 0.02, $t = 2.78$, $p < 0.008$). The distribution of genotypes, GG versus A-carriers, was not significantly different between high and low maternal overprotection (X^2 (1) = 1.51, ns). No main effect of genotype or other interactions with genotype were significant. Maternal overprotection was negatively associated with the Instagram SDI for A-carriers ($t(24) = -2.72$, df = 22, $r = -0.50$, $p = 0.0125$), but positively associated with the Instagram SDI for G/G homozygous ($t(33) = 0.61$, df = 31, $r = 0.11$, ns) (Figure 6). Although only one Pearson's r was significant, the difference between the slopes for G/G and A-carriers, calculated with Fisher's z, was statistically significant ($z = -2.32$, $p = 0.02$). Moreover, one tailed post-hoc Student's t tests on the A-carriers versus G/G in low and high maternal overprotection groups (corrected $\alpha = 0.017$) revealed that the SDI was not significantly different between A-carriers and G/G homozygotes when they reported a past of low maternal overprotection ($t = 1.79$, df = 27, $p = 0.04$, $d = 0.67$), as well as a past of high maternal overprotection ($t = -1.79$, df = 26, $p = 0.04$, $d = 0.73$) (Figure 6). No significant difference was found on A-carriers between low and high maternal overprotection ($t = 2.32$, df = 22, $p = 0.03$, $d = 0.98$) (Table 3.5). The homogeneity of variance of the SDI by maternal overprotection was verified ($K^2(1) = 3.16$, ns).

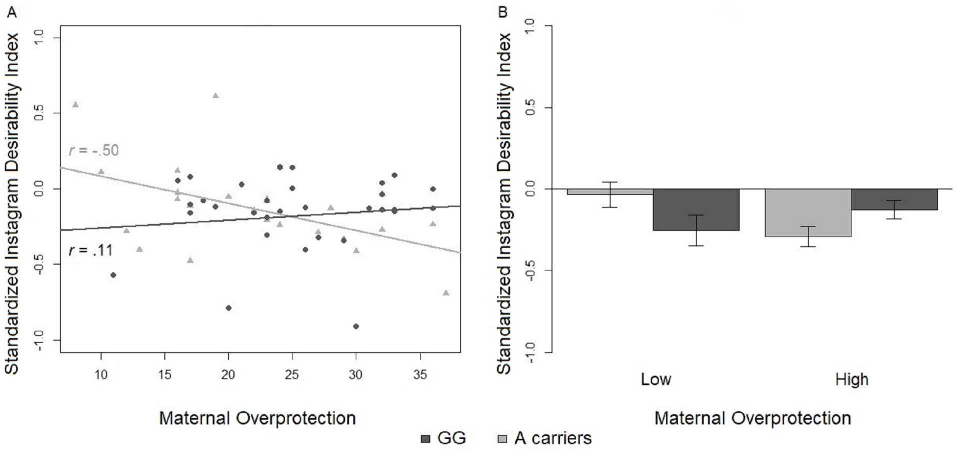

Figure 6: (**A**) Effect of the interaction between maternal overprotection and genotype on the standardized Instagram Social Desirability Index. Correlations between the Social Desirability Index and the reported maternal overprotection. Black circles = G/G homozygotes; grey triangles = A-carriers. Lines constitute the linear models for G/G homozygotes (black) and A-carriers (grey). r-values refer to Pearson's r correlations. (**B**) Comparison between the Social Desirability Index in G/G homozygotes (black) and A-carriers (grey) divided into high and low maternal overprotection.

Number of Instagram Followings and Followers

No significant main effects of the covariate, main effect of genotype, or interactions with genotype were found.

3.3.3 Instagram Effects: *OXTR* rs53576

No significant main effects of the covariate or genotype were identified. Contrary to the proposed hypothesis, no significant interactions between maternal care, maternal overprotection, paternal care, or paternal overprotection and *OXTR* rs53576 were found.

3.4 Discussion

This study investigated how alleles in *OXTR* rs2254298 and rs53576 interact differently with parental care and overprotection during childhood in explaining Instagram social behavior. Two genotype*environment interactions (*OXTR* rs2254298 SNP * parental bonding in childhood; *OXTR* rs53576 SNP * parental bonding in childhood) on the number of

Instagram followings and posts were hypothesized.

In line with the hypotheses in this study, adult Instagram users with a genetic risk factor (*OXTR* rs2254298 G/A or A/A genotype) show differential Instagram social activity according to their own early experience with parents. In particular, A-carriers, when exposed to a less optimal early environment (represented by low scores in parental care), showed a lower number of Instagram posts compared to less vulnerable genetic carriers (G/G homozygotes). Interestingly, A-carriers with a reported history of maternal overprotection also showed a decreasing trend in the Instagram SDI, whereas those with low scores in maternal overprotection showed an increasing trend in the same index. Overall, A-carriers who experienced negative patterns of interactions with their caregiver in childhood, as indicated by low paternal care and high maternal overprotection, exhibited weakened social responses on Instagram. From an analytical view, both interaction effects were found to survive the magnitude of the Bonferroni correction, which was differentially applied for the predicted (i.e., on the number of Instagram posts) and exploratory analysis (i.e., on the Instagram SDI).

These results corroborate the literature, which highlights the interaction effects between genetic predispositions and early social behaviors on human development. The moderating impact of genetics on environmental effects over Instagram social activity underpins the Susceptibility Hypothesis (Belsky, 2013). Within this framework, researchers have asserted that humans less susceptible to the environment (*OXTR* rs2254298 G/G homozygotes) will be less affected by stressful and negative conditions, but also by calming and positive events (Belsky et al., 2009). In contrast, in terms of conditional adaptation, humans with higher biological innate environmental susceptibility (*OXTR* rs2254298 A-carriers) display two dissociated behavioral patterns in relation to the quality of their early caring experiences and the consequent psychosocial outcomes (Costa et al., 2009; Boyce and Ellis, 2005; McQuaid et al., 2016): (a) if exposed to a maladaptive environment and met with strenuous adversities, these individuals would show poorer sociable attitudes towards conspecifics compared to less susceptible individuals; (b) if exposed to an adaptive environment and functional experiences, these individuals would show higher functional social characteristics in the course of development and would cope better with stressful events compared to less sensitive individuals (Belsky et al., 2007; Belsky and Pluess, 2009b; Esposito et al., 2017c).

In connection with the present findings, the G allele predisposes users to be less vulnerable, but also less plastic to the environment, thus displaying a relatively fixed Instagram social pattern less associated with the quality of early parental caregiving; whereas the A allele increases the vulnerability to the environment and moderates online social behavior: (a) individuals with low paternal care are less social users (in terms of low number of posts) than G/G homozygotes on Instagram; (b) individuals with low maternal overprotection show an opposite trend of general sociability (in terms of high SDI) compared to G/G homozygotes on Instagram. However, it is important to specify the parameters from which a differential level of sociability as a function of the two cross gene*environment interactions can be inferred.

Firstly, A-carriers with low paternal care posted less than G/G homozygotes. A plausible argument is that lower paternal care could have determined decreased abilities in coping with Instagram's overstimulating and socially demanding environment. In turn, less adaptive online behaviors could be explained by users': (a) reluctance to be a proactive agent of the social network; (b) reluctance to be exposed to others' judgment or influence (Sannon et al., 2019; Besser and Priel, 2011). An alternative explanation could be that these users are not interested in self-promotion or the development of social ties by posting (Marcus, 2015).

Secondly, A-carriers with high levels of maternal overprotection showed a decreasing trend in the Instagram SDI, whereas the opposite pattern was observed in A-carriers with lower levels of maternal overprotection. The SDI was calculated to estimate the asymmetry between the number of followers and followings for each Instagram account. Here, a history of high maternal overprotection, potentially linked to the repression of child's emotional expressions and autonomy (Mikulincer and Shaver, 2007), could shape the structure of the Instagram user's social network: the higher the SDI, the higher the number of followers at the expense of the number of followings, the higher the recognition that each user receives from other Instagrammers. This being said, a higher grade of social desirability could be more likely achieved with increased self-management (Jackson and Luchner, 2018), more intense online activity, and the ability to attend to followers' requests or expectations (Ferrara et al., 2014), thus all attitudes that could be undermined by high levels of maternal overprotection experienced in childhood (Ershad and Aghajani, 2017; Jenkins-Guarnieri et al., 2012). To conclude, Instagram users were affected by their reported paternal bonding, as well as maternal bonding. The detection of interaction effects that included one dimension for each parent provides a more balanced representation of the potential contribution of the parents in caregiving behavior.

Nevertheless, no significant interaction effects between *OXTR* rs53576 and parental bonding in childhood on Instagram social behaviors were detected. This result prompted us to elaborate on the following reasons. At a pragmatic level, different from rs2254298, the distribution in the sample for rs53576 A/A homozygous and G-carriers did not find total correspondence with the range of averaged distributions of these genotypes in the general Asiatic population. There could be indeed a remarkable variability in the alleles' frequency in the Asiatic population, for example between East and South Asia[8]. Concerning this, it is arduous to ascertain the genetic distribution in a country like Singapore. At a more theoretical level, although there are several pieces of evidence of correlations between rs53576 polymorphism and pro-social tendencies and empathy (Yamasue, 2013; Rodrigues et al., 2009), rs53576 could be

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[8] 1000 Genomes project, BioSamples: SAMN07486027-SAMN07486024, dbSNP Short Genetic Variations), 2017

more related to other explicit forms of sociality than online sociality itself. This statement could find support from two meta-analyses (Bakermans-Kranenburg and van IJzendoorn, 2008; Li et al., 2015), which found a lack of association between rs53576 and general sociality. These considerations, taken together, could point to further investigation on the specific functionality of the single-nucleotide polymorphism in the region of rs53576.

Good caregiving practices could boost social approach, even in SNSs. In light of these considerations, oxytocin receptor gene polymorphisms (rs2254298) and early caregiving behaviors contribute to the modulation of Instagram user behavior. These findings shed light on a specific side of social behavior: an online social marker of the interaction between genetic and environmental factors.

Chapter 4

How does adult attachment interact with genetic factors in moderating online social attitudes?

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[0] Chapter based on a preregistered and published study:

Study 3. Carollo, A., Bonassi, A., Cataldo, I., Gabrieli, G., Tandiono, M., Foo, J. N., Lepri B., Esposito, G. (2021). The relation between Oxytocin Receptor Gene polymorphisms, adult attachment and Instagram sociability: An exploratory analysis. *Heliyon*, 7(9), e07894. DOI: 10.1016/j.heliyon.2021.e07894.

The research presented in this chapter is linked to the following published studies of the research project:

Study E. Bonassi, A., Carollo, A., Cataldo, I., Gabrieli, G., Tandiono, M., Foo, J. N., Lepri B., Esposito, G. (2021). Modulation of Instagram Number of Followings by Avoidance in Close Relationships in Young Adults Under a Gene x Environment Perspective. *International journal of environmental research and public health*, 18(14), 7547. DOI: 10.3390/ijerph18147547.

Study F. Bonassi, A., Cataldo, I., Giulio, G., Foo, J. N., Lepri, B., Gianluca, E. (2020). Serotonin transporter gene polymorphisms and confidence in adult relationships affect the number of followed people on Instagram. *European Neuropsychopharmacology* 40(1), S385-S386. DOI: 10.1016/j.euroneuro.2020.09.500.

4.1 Introduction

As learnt from previous chapters, people forge social bonds throughout their life, from the first sight of their primary caregiver to the affection felt for their partner. Social attitudes not only have a re-creative value, but they are also crucial for the development of social and life skills. In the human life course, socialization's origins have been traced back to the interplay between genes and environment.

4.1.1 The Role of the Oxytocin Receptor Gene on Socialization

Social behavior finds its origins in the biological roots of the individual starting from the genetic predispositions. In the field of behavioral genetics on sociability, some authors have focused on the genes that rule the levels of oxytocin regulated by the *OXTR*. As described in Chapter 1, oxytocin is a neuropeptide that plays a crucial role for social skills in mammals (Bielsky and Young, 2004; Domes et al., 2007; Heinrichs and Domes, 2008; MacDonald and MacDonald, 2010; Wermter et al., 2010; Jurek and Neumann, 2018; Grinevich and Neumann, 2020). Oxytocin has a primary effect on the parental motivation towards the offspring: oxytocin plasma levels in mothers and fathers are correlated with positive engagement in parent-infant interactions consequently influencing the infant's socio-emotional development (Feldman, 2007, 2012; Young, 2014). As candidate substrates of early and long term epigenetic changes and mediators of caregiving affect social behavior throughout human development (Young, 1999; Theodosis and Poulain, 2001), oxytocin receptors are mapped in brain areas that are typically involved in reproductive, social and adaptive behaviors, such as the limbic system and the brainstem (Carter, 2003; Veening et al., 2015). Higher oxytocin levels could reinforce social experiences by causing a reduction in the levels of anxiety (Heinrichs et al., 2003; Ellison and Gray, 2009). As explained in Chapter 3, numerous *OXTR* SNPs, such as *OXTR* rs53576 and *OXTR* rs2254298, have been shown to predict parenting behaviour and attachment (Chen et al., 2011a; Feldman et al., 2012; Walum et al., 2012; Pearce et al., 2018; Julian et al., 2019). For instance, the G allele of *OXTR* rs53576 is associated with increased parental responsiveness (Bakermans-Kranenburg and van IJzendoorn, 2008), whereas the same allele on *OXTR* rs2254298 is linked to lower plasma oxytocin and to less parental touch (Rilling and Young, 2014).

Different theoretical frameworks have been proposed to provide an explication of sociability under a gene-by-environment perspective. In the intersection of hereditary factors and environmental triggers which shape human development, the Social Salience Hypothesis of oxytocin (Kemp and Guastella, 2011; Tabak, 2013) attributes distinctive social behavioral patterns associated with different *OXTR* alleles to the perceived cues of a given social environment (Striepens et al., 2012; Wittfoth-Schardt et al., 2012). An intriguing view is also offered by the Differential Susceptibility model (Belsky, 1997, 2005), which stipulates that the susceptibility to the environment depends on the so-called “plasticity genes”. These genes (e.g., *OXTR*) lead to broader individual plasticity. In fact, given a specific allele, individuals would not only show amplified adverse effects when exposed to a negative environment (Monroe and Simons, 1991; Zuckerman and Riskind, 2000), but also they would experience greater benefit from a positive and healthy environments (Esposito et al., 2018; Truzzi et al., 2017).

The two distinct *OXTR* rs53576 and *OXTR* rs2254298 SNPs appear to be favourable candidates when looking for the genetic modulation of social behavior and cognition (Kumsta and Heinrichs, 2013; Cataldo et al., 2018b). Specifically, a given allele within each of the two genetic regions could confer a peculiar level of vulnerability or susceptibility, either in an adaptive or in a maladaptive direction, to the environment in the individual (Krueger et al., 2012).

4.1.2 Environmental Influences on Socialization and Their Interplay with the Oxytocin Receptor Gene

Among multiple factors that shape sociability, environmental influences such as familiar education, parental bonding and adult attachment play a role in regulating in-person and online sociability (Lee and Chae, 2007; Yaakobi and Goldenberg, 2014; Blackwell et al., 2017; Flynn et al., 2018; Sampasa-Kanyinga et al., 2020). According to the prototypical hypothesis of attachment, the relational patterns with peers and the partner are influenced by the early relationships with parents during infancy and childhood, which appear to be stable throughout life (Griffin and Bartholomew, 1994; Feeney, 1996; Hamilton, 2000; Cataldo et al., 2021a). Nevertheless, the revisionist hypothesis points to the evidence that the adult relationships may alter the early attachment representations and form new attachment models based on the novel social experiences (Jorgensen-Wells et al., 2021). Similarly, the quality of adult relationships with peers and one's partner affects different domains of life. In fact, people from high-quality marriages (i.e., people who show better marital adjustment and higher marital satisfaction) manifest better physical and mental health than the ones in low-quality marriages (Coombs, 1991; Cotten, 1999; Simon, 2002; Holt-Lunstad et al., 2008; Braithwaite et al., 2010; Santini et al., 2015). Within the context of gene-environment interactions, multiple studies focused on social behavior as a product of a differential genetic sensitivity (i.e., *OXTR* rs53576; *OXTR* rs2254298) to positive and negative environments, such as successful or dysfunctional relationships with a partner. Previous works reported that people with the G allele of the *OXTR* rs53576 are more sensitive to hostile environments seeking higher social support when compared to the A allele (Kim et al., 2010; McQuaid et al., 2015). Individuals carrying G/G genotype or having a partner with G/G genotype also reported higher marital satisfaction than A-carriers (Monin et al., 2019). With regards to *OXTR* rs2254298, the debate on the role of vulnerability genes is still open. In fact, if on one side G/G genotype has been observed to be highly associated with separation anxiety and depression (Costa et al., 2009), on the other, females G/G homozygotes showed less attachment anxiety than A-carriers, while male G/G homozygotes exhibited less autism-associated traits than A-carriers (Chen and Johnson, 2012). The majority of studies consider A/A genotype as the one conferring the vulnerability to the environment when adopting the Differential Susceptibility Model (Thompson et al., 2011; Esposito et al., 2017e).

However, there is a paucity in research investigating online sociability, particularly those considering the continuous and reciprocal interaction between the environment to which a person is exposed and their genetic profile (Bonassi et al., 2020b,c).

4.1.3 Sociability in the context of Social Networks Sites

Nowadays, socialization takes place both offline and online, persuading researchers to examine not only the in-person social interactions but also virtual social interactions. The last decade has observed an increasing number of studies inspecting numerous social networks sites (SNSs), such as Instagram, Facebook, Twitter, whose centrality in human life has grown impressively (Seabrook et al., 2016; Kuss and Griffiths, 2017). These digital environments have become the theatres of novel and interactive social behaviors, instantly shared with large communities from all over the world.

Among the SNSs, Instagram proved to be a useful platform to explore online sociability (Ferrara et al., 2014; Wong et al., 2019). Here, users connect by posting pictures and daily stories, following other users' profiles and chatting with them actively. The studies investigating online sociability on Instagram have detected both positive (e.g. decreased feelings of solitude or increased motivation and inspiration) (Pittman and

Reich, 2016; Meier and Schäfer, 2018) and negative effects, usually linked to poorer mental health outcomes on users (Rosenquist et al., 2011; Lowe-Calverley and Grieve, 2020).

Although there is a growing number of studies on SNSs such as Instagram, it is not yet clear whether in-person and online social interactions share the same mechanisms. To fill this existing gap in the literature, the current paper aims to adopt a gene*environment perspective to investigate Instagram sociability. Specifically, the current exploratory research focuses on Instagram sociability as a result of potential interaction between genetic factors (i.e. Oxytocin Receptor Gene) and the environmental effects related to the quality of adult relationships with their partners (i.e. adult attachment with an intimate partner). Specifically, two *OXTR* SNPs (*OXTR* rs53576 and *OXTR* rs2254298) were selected as genetic factors. The Experience in Close Relationships-Revised (ECR-R) questionnaire was used to assess the individual's self-perception of adult attachment with an intimate partner (Esbjørn et al., 2015). Three Instagram variables were collected: 1) the number of posts, 2) the number of followed people (here called "followings") and the number of followers. An index, called "Social Desirability Index" (SDI), was computed as the ratio of followers to followings. Higher values of the SDI would indicate greater online sociability.

In line with the Differential Susceptibility Model, an interaction effect between the genetic factors and the close relationship scores was hypothesized for each Instagram variable. Specifically, regardless of gender, we formulated one hypothesis: *OXTR* rs2254298 A-carriers and *OXTR* rs53576 G-carriers would show a higher number of posts and values of SDI when involved in a positive and favorable relationship with their partner (lower scores in the ECR-R dimensions Avoidance and Anxiety) compared to *OXTR* rs2254298 G/G homozygotes and *OXTR* rs53576 A/A homozygotes. Conversely, *OXTR* rs2254298 A-carriers and *OXTR* rs53576 G-carriers would show a lower number of posts and SDI when involved in a negative and unfavorable relationship with their partner (higher scores in the ECR-R dimensions Avoidance and Anxiety) compared to *OXTR* rs2254298 G/G homozygotes and *OXTR* rs53576 A/A homozygotes.

4.2 Methods

4.2.1 Participants

Sixty-one (N = 61) non-parent adults were recruited among students students enrolled at the Nanyang Technological University (Singapore). Participants of the study were all Singaporean. Exclusion criteria were: (i) present or lifetime history of psychiatric, neurological or genetic disorders, (ii) not having an Instagram account, and (iii) being older than 30 years. This third criterion was adopted in order to get a pool of comparable data from participants in the same age range. It is to note that this criterion did not affect the distribution of genetic and attachment data, and reflected anyway the majority of the examined university population. We could not take into account data from four (N = 4) participants because of failures in either the online compilation of questionnaires or in Instagram data extraction. In the end, our final sample consisted of 57 adults (16 males) between 18 and 25 years-old (M = 20.89, SD = 1.59; Males: M = 22.56, SD = 1.15; Females: M = 20.24, SD = 1.24).

4.2.2 Data Collection

The methods and analytic plan for this study were preregistered on the Open Science Framework[1]. Genetic, behavioral and Instagram data were collected[2] With regards to genetic data, a sterile cotton swab for genotyping was used to collect a buccal mucosa sample of DNA from

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[1] The public registration of this study can be found on the Open Science Framework at the following address: https://osf.io/t78fu

[2] The research was authorized by the Ethical Committee of Nanyang Technological University (IRB-2015-08-020-01). Informed consent was obtained from all participants. The study followed the Declaration of Helsinki. The genetic assessment was conducted on anonymized samples at the Nanyang Technological University (Singapore). Instagram data and questionnaires' data were anonymized at the beginning of the data collection.

each participant. Concerning the behavioral assessment, every participant completed online the self-report questionnaire Experience in Close Relationships-Revised (ECR-R). To collect Instagram indexes, an inhouse built Python-based web-scraper developed on BeautifulSoup, a python package designed for web-scraping (Richardson, 2007), was employed. Firstly, the algorithm extracted the content of participants' Instagram profile from the DOM of the page. Subsequently, the algorithm detected the specific objects âĂŤnamely "posts", "followers", and "following" âĂŤ in order to limit the amount of personal information accessed from each profile. A manual inspection of the data was then conducted to check for the presence of missing values due to technical errors, which were then manually updated (e.g. connection timeout, server errors). The same script was employed in previous works (Bonassi et al., 2020b). The final dataset generated for this work is available online on the Data Repository of the Nanyang Technological University (DR-NTU Data) (Gabrieli et al., 2020).

4.2.3 Genetic assessment

The genetic assessment of the present study employed the method reported by Bonassi et al. (2017). DNA extraction and genotyping were performed by ACGT, Inc. (Wheeling, IL). DNA was extracted by using Oragene DNA purification reagent and its concentrations were evaluated through spectroscopy (NanoDrop Technologies, USA). Each DNA sample was increased by polymerase chain reaction (PCR) for the *OXTR* gene rs53576 region target with the primers 5-GCC CAC CAT GCT CTC CAC ATC-3 and 5-GCT GGA CTC AGG AGG AAT AGG GAC-3. A PCR reaction of 20 ll, comprising 1.5 ll of genomic DNA from the test sample, PCR buffer, 1 mM each of the forward and reverse primers, 10 mM deoxyribonucleotides, KapaTaq polymerase, and 50 mM MgCl2 was executed. PCR operation comprised of 15 minute denaturation at 95 °C, and 35 cycles at 94 °C (30 s), 60 °C(60 s), 72 °C (60 s) and a final 10 minute step at 72 °C. PCR reactions were genotyped with an ABI

3730xl Genetic Analyzer[3] and normalized with GeneScan 600 LIZ[4] size standards on each sample. Genotypic data were inspected using GeneMapper ID[5].

The same procedure was used to assess the *OXTR* gene rs2254298 region. However, the forward and reverse primers were instead 5-TGA AAG CAG AGG TTG TGT GGA CAG G-3 and 5-AAC GCC CAC CCC AGT TTC TTC-3 respectively.

4.2.4 Close Relationships

In order to assess the participants' relationship with their partner, the Experience in Close Relationship-Revised questionnaire was used. Developed by Fraley et al. (2000b), the ECR-R (average CronbachâĂŹs $\alpha = 0.89$) is a 36-item self-report questionnaire on a 7-point response scale, that examines the close relationship across two dimensions: Anxiety (CronbachâĂŹs $\alpha = 0.93$) and Avoidance (CronbachâĂŹs $\alpha = 0.85$). While the former is usually linked to worries about the relationship, and fear of rejection from one's partner (i.e., "I find that my partner(s) don't want to get as close as I would like"), the latter mostly refers to discomfort with intimacy and closeness to one's partner (i.e., "I find it difficult to allow myself to depend on romantic partners"). The current instrument has obtained extensive approval, high reliability and adequate consistency in appraising the constructs related to the attachment styles with the romantic partner (Sibley et al., 2005; Cameron et al., 2012; Busonera et al., 2014b). Several studies applied the ECR-R to understand how the adult attachment security can be modulated by infant attachment, childhood maltreatment and can moderate social cognition, emotional regulation, personality and mindfulness (Mikulincer and Shaver, 2007; Hocking et al., 2016; Nielsen et al., 2017b; Baryshnikov et al., 2017). The ECR-R has also been used by researchers in the field of behavioral genetics dimensions were, were conceived as potential environmental vari-

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[3] Applied Biosystems Inc.

[4] Applied Biosystems, Inc.

[5] Applied Biosystems, Inc.

ables able to affect physiological and psychological variables (Donnellan et al., 2008), or the product of gene*environment interactions (Török and Vincze, 2015; Cataldo et al., 2020). We calculated the scores for the two constructs of anxiety and avoidance by following the scoring indications reported by (Picardi et al., 2002).

4.2.5 Instagram Variables

Four variables were considered as highly representative of online sociability on Instagram. Number of posts indicates the number of content published by a participant's profile. On Instagram, the number of posts is equivalent to the number of published pictures, since this social network allows accounts to publish pictures and video with an auxiliary text. The literature regarding the determinants of one's number of posts shows contrasting results. For instance, depressed mood can be an antecedent of an increased posting activity as well as narcissism, or even extraversion (Moon et al., 2016; Frison and Eggermont, 2017; Bowden-Green et al., 2020). Therefore, an increased activity on SNSs is not a mere positive or negative indicator of the user's well-being, but may depend on diverse and even contrasting drives (e.g., the need to escape from reality, the need to get in touch with others, and so on). The number of followed people ("followings") is an index that reflects the number of profiles that a participant follows. On Instagram, following allows the user (the follower) to view âĂŤ or ask to view, in the case of private profiles âĂŤ other users' posts (the "followings") in the general feed. Conversely, the number of followers is defined by the number of profiles that follows the considered participant. Broadly speaking, publishing a post can be considered as an active form of social communication, for the user decides what others can see from their profile. Following, instead, is a type of passive communication, for the user is exposed to the contents selected by others. Additionally, the SDI was computed as the ratio of followers to followings. This parameter, previously adopted as a measure of general sociability (Bonassi et al., 2020b,c), estimates the balance between the number of followers and followings for each account. By simultaneously taking into account the amount of profiles that one follows or is followed by, the SDI can furnish an estimate of the centrality of a specific user within the network of contacts. SDI can theoretically range from 0 to infinite, where 0 indicates a strong interest on following other people's contents and infinite indicates a scarce interest on following other accounts together with a strong appeal for other people. Values close to 1 for SDI would indicate a balanced activity in the network, ideally with the same values of followers and followings.

4.2.6 Statistical Analysis

Statistical analysis and data visualization were performed using R (R-core base version 4.0.0.). Instagram data were standardized using z-score transformation and visually inspected for normality. To reduce the variability of the data, and to increase the statistical power of performed tests (Erceg-Hurn and Mirosevich, 2008; Leys et al., 2019), outliers âĂŤ defined as values that differ by two or more standard deviations from the mean of the distribution - were inspected in the database. Overall, 8 data point were identified as outliers (3 for followings number, 2 each for posts number and SDI, 1 for follower number).

Normality of ECR-R and Instagram scores were tested by computing the values of skewness and kurtosis and their distributions were manually inspected by visualization via boxplots, density plots, and quantile-quantile plots. Of the investigated variables, the participant's number of posts did not follow the Gaussian distribution. Thus, the related sampling was adjusted and log-transformed. Subsequently, the assumption of the homogeneity of variance was verified.

To detect potential gene*environment interactions on Instagram variables considered for the two hypotheses (number of posts, SDI values), two different mixed ANCOVAs were employed for each *OXTR* gene SNP: one ANCOVA with Instagram number of posts and one with Instagram SDI as DV for *OXTR* rs53576, whereas one ANCOVA with Instagram number of posts and one with Instagram SDI as DV for *OXTR* rs2254298 (Alexander et al., 2009; Esposito et al., 2017e; Truzzi et al., 2018). To take into account the increased possibility of committing a type I error, a false discovery rate correction was employed by means of a Bonferroni Correction (corrected $\alpha = 0.025$). Bonferroni's method for multiple testing correction was chosen rather than the available alternative approaches to apply a more conservative correction.

A prior sensitivity power analysis conducted on G*Power (Faul et al., 2009) (power = 0.80) estimated that the analysis could detect a medium effect size (f = 0.42) via analysis of covariance given the current sample size ($N = 57$) and the corrected $\alpha = 0.025$ (ANCOVA: fixed effects, main effects and interactions).

In the analysis, *OXTR* rs53576 (A/A vs. G-carriers) and *OXTR* rs2254298 (G/G vs. A-carriers) were considered as separate predictors in distinct analyses. Two out of four mixed ANCOVAs included the *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates, as in Equation 4.1.

$$Instagram_variable = OXTRSNP * (ECR_Anxiety + ECR_Avoidance) \tag{4.1}$$

Likewise, the two remaining ANCOVAs included the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as the between-subject factor, and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates, as in Equation 4.1. If any significant difference emerged on the values of the Instagram variables in relation to the participants' gender, gender was included in the ANCOVA equation as a between-subject factor.

4.3 Results

4.3.1 Results observed on unaltered data

Preliminary Analysis on the Genetic Variables

As common practice in the genetic studies, in order to have statistically comparable groups of participants, the heterozygotes and less numerous homozygotes groups were merged together in a group of "allele-carriers" (Truzzi et al., 2018). Therefore, within the *OXTR* rs53576 DNA region, participants with at least one G allele (G/G homozygotes or A/G) were categorized into a single G-carriers group. The distribution in our sample was 39% for A/A homozygous and 61% for G-carriers. The frequencies of the genotype were: A/A = 22 (38.60%), A/G = 30 (52.63%), G/G = 5 (8.77%), and the distribution was consistent with the Hardy-Weinberg Equilibrium (X^2 (1) = 1.38, p = 0.241, ns). For the *OXTR* gene rs2254298 region, participants with at least one A allele (A/A homozygotes or G/A) were classified into a single A-carriers group. The distribution in our sample was 56% for G/G homozygotes and 44% for A-carriers. The frequencies of the genotype were: A/A = 4 (7.02%), G/A = 21 (36.84%), G/G = 32 (56.14%), and the distribution was consistent with the Hardy-Weinberg Equilibrium (X^2 (1) = 0.05, p = 0.828, ns). Table 4.1 reports the observed frequency of *OXTR* rs53576 and *OXTR* rs2254298 genotypes by the total sample size. In the context of *OXTR* rs53576, participants gender ($X^2(1) = 0.17$, $p = 0.683$, ns) did not significantly differ between the two groups A/A vs G. As regards *OXTR* rs2254298, participants' gender ($X^2(1) = 0.81$, $p = 0.367$, ns) did not significantly differ between the two groups G/G vs A.

Preliminary Analysis on ECR-R and Instagram Variables

Table 4.2 describes the values concerning the data distribution of each continuous variable (two ECR-R dimensions and four Instagram variables) in terms of skewness, kurtosis and descriptive statistics (see "Sta-

OXTR rs53576	
Alleles	**Total**
AA	22 (38.60%)
AG	30 (52.63%)
GG	5 (8.77%)
G-carriers	35 (61.40%)
Total	57
OXTR rs2254298	
Alleles	**Total**
AA	4 (7.02%)
GA	21 (36.84%)
GG	32 (56.14%)
A-carriers	25 (43.86%)
Total	57

Table 4.1: Frequency values of the total sample in Oxytocin Receptor Gene (*OXTR*) rs53576 and Oxytocin Receptor Gene (*OXTR*) rs2254298 genotypes. The frequency percentage of each genotype is reported between parenthesis. The presented allelic frequencies are consistent with the Hardy-Weinberg equilibrium (for *OXTR* rs53576, X^2 (1) $= 1.38$, $p = 0.241$, ns; for *OXTR* rs2254298, X^2 (1) $= 0.05$, $p = 0.828$, ns). The present data refer to the 57 participants which completed the entire assessment across three levels: genetic (*OXTR* rs53576; *OXTR* rs2254298), behavioral (Experience in Close Relationships-Revised questionnaire) and Instagram (number of posts, following, followers, and the Social Desirability Index) data collections.

tistical Analysis" for further details).

Variable	**Skewness**	**Kurtosis**	**Min**	**1st Q**	**Median**	**Mean**	**3rd Q**	**Max**	**SD**
Anxiety	-0.38	-0.02	1.39	3.33	3.94	3.94	4.56	6.22	1.08
Avoidance	-0.15	-0.39	1.06	2.11	2.94	2.95	3.67	5.39	0.93
Posts number	3.43	12.61	-0.60	-0.51	-0.36	0.00	0.04	4.61	1.00
Log-transformed posts number	2.08	4.78	0.33	0.40	0.49	0.62	0.71	1.89	0.34
Social Desirability Index	5.66	35.39	-1.16	-0.27	-0.12	0.00	0.01	6.76	1.00
Log-transformed Social Desirability Index	2.28	12.73	-0.17	0.55	0.63	0.64	0.70	2.17	0.29
Followings	0.53	-0.46	-1.53	-0.77	-0.12	0.00	0.67	2.47	1.00
Followers	4.74	27.70	-0.80	-0.50	-0.17	0.00	0.24	6.40	1.00
Log-transformed followers number	1.71	5.84	0.18	0.40	0.61	0.63	0.81	2.13	0.33

Table 4.2: Summary of the descriptive statistics for each continuous variable. The distribution of each ECR-R (Experience in Close Relationships-Revised) dimension and Instagram variable is described in terms of Skewness, Kurtosis, Minimum (Min), first Quartile (1st Q), Median, Mean, third Quartile (3rd Q), Maximum (Max) and Standard Deviation (SD). Instagram variables were standardized using z-score transformation and inspected for normality. Skewness and Kurtosis values were computed for each continuous subscale of the ECR-R questionnaire and each Instagram variable. Participants' number of posts, Social Desirability Index, and number of followers did not follow the Gaussian distribution, and were thus adjusted by log-transformation.

To exclude any significant effect of participants' gender on Instagram variables, four preliminary two-tailed Student's t-tests were performed (corrected $\alpha = 0.0125$). As expected, no significant differences in the standardized Instagram number of posts (t = *-0.16, df = 55,* p = *0.874),* *95% CI [-0.22, 0.18]*, followings (t = 2.20 df = 55, p = 0.032), 95% CI [0.06, 1.20], and on the standardized SDI (t = 1.60, df = 55, p = 0.116), 95% CI [-0.03, 0.31] were found between male and female participants. Conversely, a significant difference between genders was detected for Instagram number of followers (t = 2.60, df = 55, p = 0.012), 95% CI [0.05, 0.42]. This evidence allows to analyze data of female and male participants together in the subsequent analysis on Instagram number of posts, followings, and SDI. As for Instagram number of followers, participants' gender was included in the subsequent analysis and examined as a potential moderator factor.

Hypothesis-Driven Analysis: Instagram Number of Posts and SDI

Means and standard error means of Instagram number of posts and SDI for *OXTR* rs53576 and *OXTR* rs2254298 are reported in Table 4.3.

***OXTR* rs53576**				
Number of Posts				
ECR-R dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.76 (0.12)	0.54 (0.05)	0.67 (0.15)	0.58 (0.07)
Avoidance	0.91 (0.15)	0.62 (0.06)	0.49 (0.04)	0.50 (0.06)
Social Desirability Index				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.59 (0.03)	0.74 (0.11)	0.63 (0.02)	0.58 (0.07)
Avoidance	0.62 (0.02)	0.66 (0.07)	0.59 (0.02)	0.66 (0.11)
***OXTR* rs2254298**				
Number of Posts				
ECR-R dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	0.60 (0.06)	0.67 (0.13)	0.67 (0.11)	0.54 (0.07)
Avoidance	0.74 (0.09)	0.74 (0.12)	0.52 (0.05)	0.48 (0.06)
Social Desirability Index				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	0.69 (0.11)	0.65 (0.05)	0.62 (0.08)	0.58 (0.04)
Avoidance	0.66 (0.06)	0.62 (0.06)	0.65 (0.13)	0.60 (0.02)

Table 4.3: Mean values in Oxytocin Receptor Gene (*OXTR*) rs53576 A/A homozygotes and G-carriers and Oxytocin Receptor Gene (*OXTR*) rs2254298 G/G homozygotes and A-carriers divided by Experience in Close Relationships-Revised (ECR-R) dimensions (high or low) on Instagram number of posts and Social Desirability Index. Standard error means are reported between parentheses. Instagram behavior is reported by users' *OXTR* rs53576 phenotype and ECR-R dimensions, consistently with the literature on the topic and a previous publication (Bonassi et al., 2020b).

Results revealed no significant main effects of *OXTR* rs53576 ($p >$

0.025) on Instagram number of posts and SDI. Nevertheless, a main effect emerged for ECR-R avoidance on the number of posts ($F(1,\ 56) = 9.96$, $p < 0.003$, p$\eta^2 = 0.16$). Moreover, a significant interaction between ECR-R avoidance and *OXTR* rs53576 on Instagram number of posts was found ($F(1,\ 56) = 7.12$, $p < 0.010$, p$\eta^2 = 0.12$). No other main effect or interaction effect was detected on the number of posts and SDI 4.4.
Similarly, when considering *OXTR* rs2254298, the same main effect of avoidance in close relationships on the number of posts on Instagram was detected ($F(1,\ 56) = 10.36$, $p < 0.002$, p$\eta^2 = 0.17$) (see Table 4.4).

To test the directionality of the effects found in the hypothesis-driven analyses, consequent post-hoc analyses were implemented. In particular, avoidance from the partner emerged to negatively predict one's number of posts on Instagram ($t(55)$ = -2.54, r = -0.32, p = 0.014, 95% CI [-0.54, -0.07]). In other words, the higher the avoidance, the lower the number of Instagram posts. Moreover, after applying the median split to the values of avoidance in close relationships, the result was confirmed by a two-tailed Student's t test. Specifically, a significant difference emerged when comparing participants with low and high values of avoidance in regards to their number of Instagram posts ($t(55) = 2.85$, $p = 0.006$, 95% CI [0.07, 0.41]) (see Figure 7).

OXTR rs53576					
Number of posts					
Variable	**DF**	**Sum Square**	**Mean Square**	***F*** **value**	***p*-value**
OXTR rs53576	1	0.338	0.3381	3.925	0.05299
Anxiety	1	0.068	0.0676	0.785	0.37972
Avoidance	1	0.858	0.8579	9.958	0.00269 **
OXTR rs53576: Anxiety	1	0.025	0.0248	0.287	0.59417
OXTR rs53576: Avoidance	1	0.613	0.6130	7.116	0.01022 *
Residuals	51	4.394	0.0861		
Social Desirability Index					
Variable	**DF**	**Sum Square**	**Mean Square**	***F*** **value**	***p*-value**
OXTR rs53576	1	0.035	0.03469	0.373	0.544
Anxiety	1	0.034	0.03417	0.367	0.547
Avoidance	1	0.000	0.00023	0.002	0.961
OXTR rs53576: Anxiety	1	0.023	0.02330	0.250	0.619
OXTR rs53576: Avoidance	1	0.004	0.00424	0.046	0.832
Residuals	51	4.748	0.09309		
OXTR rs2254298					
Number of posts					
Variable	**DF**	**Sum Square**	**Mean Square**	***F*** **value**	***p*-value**
OXTR rs2254298	1	0.014	0.0144	0.146	0.70366
Anxiety	1	0.034	0.0341	0.348	0.55801
Avoidance	1	1.017	1.0172	10.358	0.00224 **
OXTR rs2254298: Anxiety	1	0.108	0.1075	1.095	0.30034
OXTR rs2254298: Avoidance	1	0.113	0.1133	1.153	0.28792
Residuals	51	5.008	0.0982		
Social Desirability Index					
Variable	**DF**	**Sum Square**	**Mean Square**	***F*** **value**	***p*-value**
OXTR rs2254298	1	0.027	0.02727	0.293	0.590
Anxiety	1	0.029	0.02887	0.311	0.580
Avoidance	1	0.001	0.00113	0.012	0.912
OXTR rs2254298: Anxiety	1	0.026	0.02594	0.279	0.600
OXTR rs2254298: Avoidance	1	0.022	0.02177	0.234	0.630
Residuals	51	4.739	0.09293		

Table 4.4: Hypothesis-driven analysis: statistics' summary of ANCOVAs on Instagram number of posts and Social Desirability Index. For each Instagram variable considered in the hypothesis (Instagram number of posts and SDI) as dependent variable, one mixed ANCOVA was performed with *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates (see the top section of the Table). For each Instagram variable, one mixed ANCOVA was also performed with the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as a between-subject factor and the other parameters unchanged (see the below section of the Table). A significant main effects of the avoidance in close relationships was found on the number of posts. Also, avoidance in close relationships by interacting with the *OXTR* rs53576 resulted to modulate the number of posts. (* $p < 0.025$; ** $p < 0.001$).

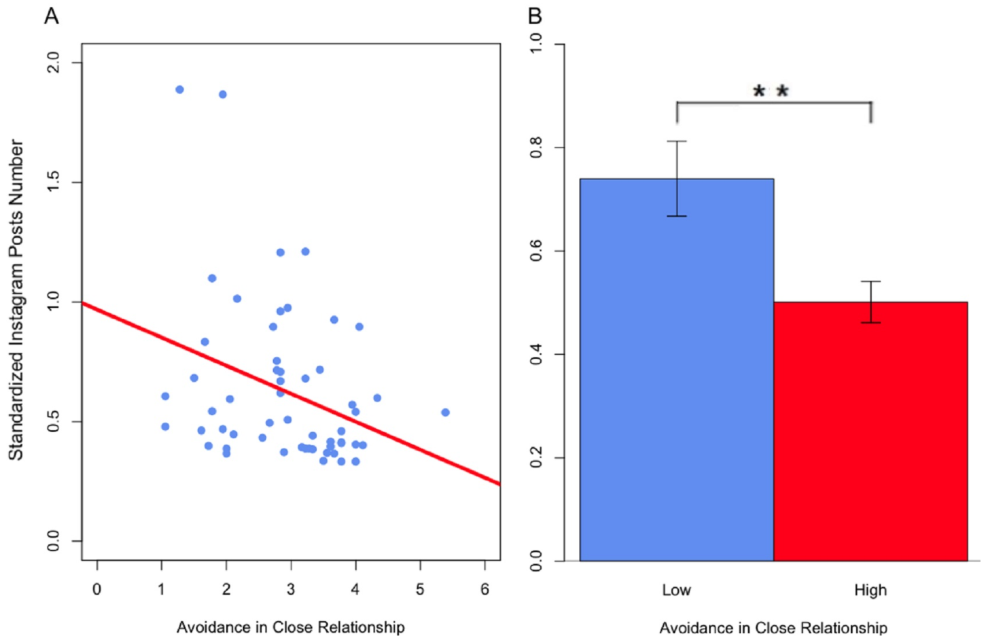

Figure 7: Main Effect of Avoidance in Close Relationships on Instagram Number of Posts. On the left, the negative linear association between avoidance and Instagram number of posts. On the right, comparison between the number of posts in participants with low (blue) and high (red) avoidance in close relationships (** $p < 0.01$).

Also the effect found for the interplay between the *OXTR* rs53576 genotype and ECR-R avoidance on the number of posts was examined with post-hoc tests. In particular, after applying the median split procedure on the ECR-R avoidance, it emerged that the distribution of genotypes (G/G vs. A-carriers groups) was not significantly different between participants showing high rather than low avoidance ($X^2(1) = 0.03$, $p = 0.867$, ns). Avoidance in close relationships resulted to be significantly correlated with the number of posts for the individual in the group of A/A carriers (t = -2.80, df = 20, r = -0.53, p = 0.011, 95% CI [-0.78, -0.14]). Conversely, the correlation between avoidance and number of posts on Instagram was not significant for the G-carriers (t = -0.22, df = 33, r = -0.04, p = 0.831, 95% CI [-0.37, 0.30]). Homogeneity of variance of the Instagram number of posts by avoidance in close relationships was checked (K^2 = 9.55, df = 1, p = 0.002) (see Figure 8).

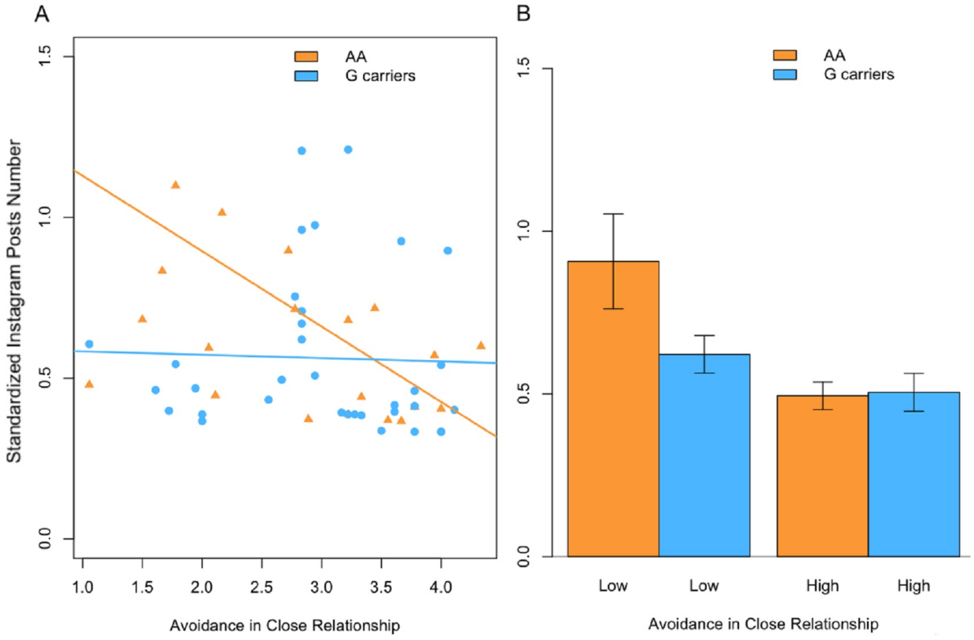

Figure 8: Interaction between Avoidance in Close Relationships and *OXTR* rs53576 genotype on determining the Instagram number of posts. On the left, linear relationships between between avoidance in close relationships and Instagram number of posts divided by genotype (in orange A/A homozygotes, in light blue C-carriers). On the right, comparison between the number of Instagram posts in participants with high and low levels of avoidance. Barplots are reported for both the genetic groups: A/A homozygotes in orange and C-carriers in light blue.

Exploratory Analysis: Instagram Number of Followings and Followers

Means and standard error means of Instagram number of followings and followers for *OXTR* rs53576 and *OXTR* rs2254298 are reported in Table 4.5.

The hypothesis-driven approach adopted for Instagram number of posts and SDI was extended as exploratory analysis to the number of followings and followers. Therefore, a Bonferroni's correction was separately applied for the two exploratory tests (corrected $\alpha = 0.025$). To identify exploratory gene*environment interactions on two further Instagram variables that were collected (number of followings and followers), two mixed ANCOVAs were employed for each *OXTR* gene SNP: one ANCOVA with Instagram's number of followings and one with Instagram number of followers as DV for *OXTR* rs53576, whereas one ANCOVA

***OXTR* rs53576**				
Number of Followings				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.78 (0.30)	-0.23 (0.19)	-0.08 (0.34)	-0.26 (0.21)
Avoidance	0.54 (0.31)	-0.04 (0.25)	0.21 (0.38)	-0.44 (0.14)
Number of Followers				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.76 (0.06)	0.67 (0.11)	0.59 (0.09)	0.52 (0.06)
Avoidance	0.72 (0.08)	0.62 (0.07)	0.62 (0.08)	0.57 (0.10)
***OXTR* rs2254298**				
Number of Followings				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	0.16 (0.27)	0.23 (0.27)	-0.21 (0.28)	-0.18 (0.23)
Avoidance	0.08 (0.26)	0.37 (0.31)	-0.12 (0.29)	-0.31 (0.16)
Number of Followers				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	0.72 (0.11)	0.68 (0.07)	0.54 (0.08)	0.55 (0.06)
Avoidance	0.63 (0.07)	0.70 (0.08)	0.64 (0.13)	0.53 (0.04)

Table 4.5: Mean values in Oxytocin Receptor Gene (*OXTR*) rs53576 A/A homozygotes and G-carriers and Oxytocin Receptor Gene (*OXTR*) rs2254298 G/G homozygotes and A-carriers divided by Experience in Close Relationships-Revised (ECR-R) dimensions (high or low) on Instagram number of followings and followers. Standard error means are indicated between parentheses.

with Instagram's number of followings and one with Instagram number of followers as DV for *OXTR* rs2254298. For each ANCOVA the between-subject factor and the covariates were unchanged, as in Equation 4.1. Moreover, since Instagram number of followers emerged to be significantly different between genders, participants' gender itself was included as a moderator factor in the ANCOVA equations regarding the number of followers.

The ANCOVA performed on Instagram number of followings revealed a significant main effect of *OXTR* rs53576 genotype ($F(1, 56) = 6.19$, $p < 0.016$, p$\eta^2 = 0.11$), as indicated in Table 4.6. No further significant interactions between the ECR-R subscales and *OXTR* rs53576 on the Instagram number of followings were observed (see Table 4.6).

To explore the direction of the ANCOVA effect, a further post-hoc two-tailed StudentâĂŹs t test was computed. The Student's t test confirmed that the number of Instagram followings was significantly different between the A/A vs G allele groups ($t = 2.45$, df = 55, $p = 0.018$, 95% CI [0.12, 1.16]; see Figure 9).

OXTR rs53576					
Number of Followings					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	5.50	5.505	6.193	0.0161 *
Anxiety	1	0.27	0.266	0.299	0.5870
Avoidance	1	1.72	1.717	1.932	0.1706
OXTR rs53576: Anxiety	1	2.37	2.369	2.665	0.1088
OXTR rs53576: Avoidance	1	0.81	0.809	0.910	0.3446
Residuals	51	45.33	0.889		
Number of Followers					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	0.095	0.0948	0.886	0.3515
Gender	1	0.712	0.7118	6.652	0.0132 *
Anxiety	1	0.132	0.1317	1.231	0.2731
Avoidance	1	0.020	0.0197	0.184	0.6699
OXTR rs53576: Gender	1	0.049	0.0485	0.453	0.5042
OXTR rs53576: Anxiety	1	0.166	0.1661	1.552	0.2192
OXTR rs53576: Avoidance	1	0.002	0.0020	0.019	0.8921
Gender: Anxiety	1	0.008	0.0077	0.072	0.7892
Gender: Avoidance	1	0.008	0.0085	0.079	0.7795
OXTR rs53576: Gender: Anxiety	1	0.003	0.0032	0.029	0.8644
OXTR rs53576: Gender: Avoidance	1	0.018	0.0182	0.170	0.6821
Residuals	45	4.816	0.1070		
OXTR rs2254298					
Number of Followings					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.01	0.0138	0.014	0.908
Anxiety	1	0.61	0.6106	0.603	0.441
Avoidance	1	2.58	2.5842	2.553	0.116
OXTR rs2254298: Anxiety	1	0.61	0.6118	0.604	0.440
OXTR rs2254298: Avoidance	1	0.56	0.5602	0.553	0.460
Residuals	51	51.62	1.0121		
Number of Followers					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.009	0.0088	0.082	0.7761
Gender	1	0.650	0.6500	6.035	0.0179 *
Anxiety	1	0.164	0.1637	1.520	0.2241
Avoidance	1	0.034	0.0344	0.319	0.5749
OXTR rs2254298: Gender	1	0.140	0.1400	1.300	0.2603
OXTR rs2254298: Anxiety	1	0.004	0.0036	0.033	0.8566
OXTR rs2254298: Avoidance	1	0.017	0.0167	0.155	0.6953
Gender: Anxiety	1	0.025	0.0253	0.235	0.6305
Gender: Avoidance	1	0.003	0.0033	0.031	0.8608
OXTR rs2254298: Gender: Anxiety	1	0.094	0.0941	0.874	0.3549
OXTR rs2254298: Gender: Avoidance	1	0.041	0.0410	0.381	0.5403
Residuals	45	4.847	0.1077		

Table 4.6: Exploratory analysis: statistics' summary of ANCOVAs on Instagram number of followings and number of followers. For each Instagram variable considered in the exploratory analysis (Instagram number of followings and followers) as dependent variable (DV), one mixed ANCOVA was performed with *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates, as in Equation 4.1 (see the top section of the Table). Gender was added as a further between-subjects factor in the analysis including Instagram number of followers. For each Instagram variable, one mixed ANCOVA was also performed with the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as a between-subject factor and the other parameters unchanged (see the below section of the Table). A gender effect on the number of followings was confirmed, and a significant main effects of the genotype was found on the number of followings. (* $p < 0.025$).

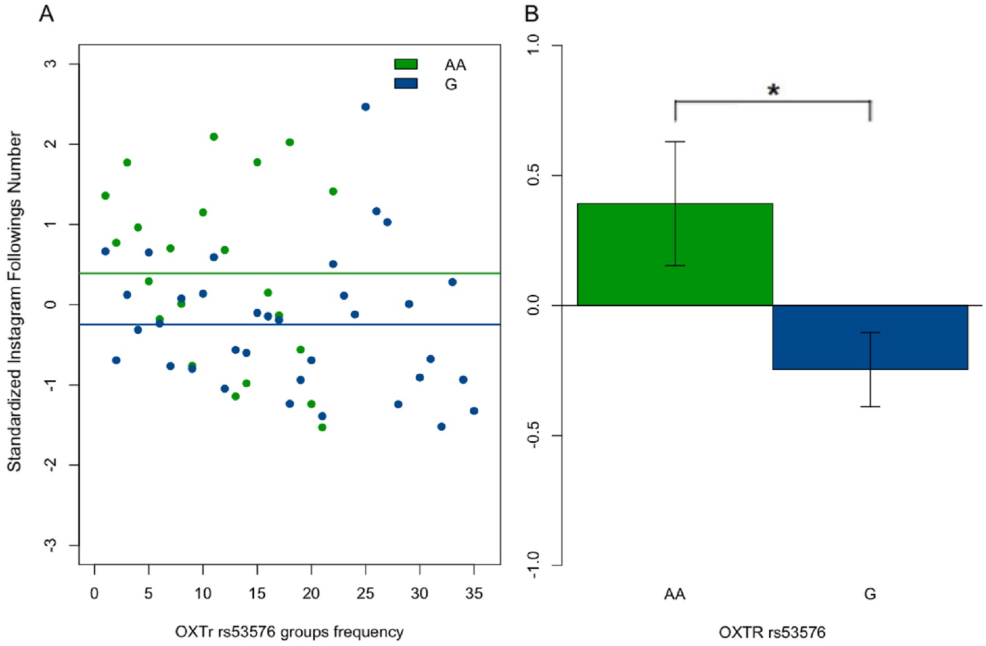

Figure 9: Main Effect of *OXTR* rs53576 on Instagram Number of Followings. On the left, effect of Oxytocin Receptor Gene (*OXTR*) rs53576 on the standardized Instagram number of followings. Green circles = A/A homozygotes; blue circles = G-carriers. Lines constitute the linear models for A/A homozygotes (green) and G-carriers (blue). On the right, comparison between the number of Instagram followings in A/A homozygotes (green) and G-carriers (blue) (* $p < 0.025$).

Besides the effect of gender on the number of followers, no other significant main effect of *OXTR* rs53576 or interaction effect between the ECR-R dimensions, gender and *OXTR* rs53576 were found on Instagram number of followers ($p > 0.025$), as reported in Table 4.6.

With regards to *OXTR* rs2254298, main effect of gender on the number of followers apart, no other significant main effect of genotype or interaction effect between the ECR-R subscales, gender and genotype was identified on Instagram number of followings or followers, as reported in Table 4.6.

4.3.2 Results obtained excluding outliers

Preliminary Analysis on the Genetic Variables

When excluding the outlier values, the genetic distributions varied in relation to the Instagram variable that was considered for the analysis. For *OXTR* rs53576, the frequencies of genotype were: A/A = 20 (36.36%), A/G = 30 (54.55%), G/G = 5 (9.09%) for the number of posts (Hardy-Weinberg Equilibrium: X^2 (1) = 1.754, p = 0.185, ns).; A/A = 22 (40.00%), A/G = 28 (50.91%), G/G = 5 (9.09%) for SDI (Hardy-Weinberg Equilibrium: X^2 (1) = 0.869, p = 0.351, ns); A/A = 22 (39.28%), A/G = 29 (51.79%), G/G = 5 (8.93%) for the number of followers (Hardy-Weinberg Equilibrium: X^2 (1) = 1.111, p = 0.292, ns); A/A = 20 (37.04%), A/G = 29 (53.70%), G/G = 5 (9.26%) for the number of followings (Hardy-Weinberg Equilibrium: X^2 (1) = 1.450, 0.228, ns). For *OXTR* rs53576, the frequencies of genotype were: A/A = 3 (5.46%), G/A = 21 (38.18%), G/G = 31 (56.36%) for the number of posts (Hardy-Weinberg Equilibrium: X^2 (1) = 0.052, p = 0.819, ns); A/A = 4 (7.27%), G/A = 21 (38.18%), G/G = 30 (54.55%) for SDI (Hardy-Weinberg Equilibrium: X^2 (1) = 0.015, p = 0.902, ns); A/A = 4 (7.14%), G/A = 21 (37.50%), G/G = 31 (55.36%) for the number of followers (Hardy-Weinberg Equilibrium: X^2 (1) = 0.029, p = 0.864, ns); A/A = 4 (7.41%), G/A = 21 (38.89%), G/G = 29 (53.70%) for the number of followings (Hardy-Weinberg Equilibrium: X^2 (1) = 0.005, p = 0.941, ns).

Preliminary Analysis on ECR-R and Instagram Variables

Considering the large amount of outliers that emerged from the previous analysis, such values were therefore removed in relation to the dependent variable of interest. In particular, when considering the number of posts in subsequent analysis, 2 participants were removed for they represented extreme values. The same number of participants was removed when considering the SDI as the dependent variable. Conversely, 3 and 1 participants were removed when considering the number of followings and followers respectively as dependent variables. Table 4.7 reports skewness, kurtosis, and descriptive statistics for the continuous variables of the study.

Again, four preliminary two-tailed Student's t-tests (corrected α = 0.0125) were computed to examine the existence of a gender effect on the Instagram variables. No significant difference between males and fe-

Variable	Skewness	Kurtosis	Min	1st Q	Median	Mean	3rd Q	Max	SD
Anxiety	-0.38	-0.02	1.39	3.33	3.94	3.94	4.56	6.22	1.08
Avoidance	-0.15	-0.39	1.06	2.11	2.94	2.95	3.67	5.39	0.93
Posts number	1.53	1.64	-0.60	-0.52	-0.39	-0.16	0.01	1.36	0.50
Log-transformed posts number	1.14	0.33	0.33	0.39	0.48	0.58	0.70	1.21	0.24
Social Desirability Index	-0.69	2.45	-1.16	-0.28	-0.13	-0.16	-0.01	0.61	0.30
Followings	0.34	-0.74	-1.53	-0.79	-0.14	-0.12	0.57	1.78	0.89
Followers	0.77	0.11	-0.80	-0.51	-0.17	-0.11	0.22	1.45	0.51

Table 4.7: Summary of the descriptive statistics for each continuous variable after removing the outliers (N = 2 for Instagram posts; N = 2 for Social Desirability Index; N = 3 for Instagram followings; N = 1 for Instagram followers) from the data pool. The distribution of each ECR-R (Experience in Close Relationships-Revised) dimension and Instagram variable is described in terms of Skewness, Kurtosis, Minimum (Min), first Quartile (1st Q), Median, Mean, third Quartile (3rd Q), Maximum (Max) and Standard Deviation (SD). Instagram variables were standardized using z-score transformation and inspected for normality. Skewness and kurtosis values were computed for each continuous subscale of the ECR-R questionnaire and each Instagram variable. Of all variables, only participants' number of posts did not follow the Gaussian distribution, and was thus adjusted by log-transformation. Log-transformed number of posts shows increased values compared to the original sampling of the same variable.

males participants' scores was detected for any of the Instagram variables (number of posts: $t = 0.68$, df = 53, $p = 0.498$, 95% CI [-0.09, 0.19]; SDI: $t = 0.90$, df = 55, $p = 0.374$, 95% CI [-0.10, 0.26]; number of followings: $t = 2.53$, df = 52, $p = 0.015$, 95% CI [0.13, 1.15]; number of followers: $t = 1.84$, df = 54, $p = 0.071$, 95% CI [-0.02, 0.58]). Thus, participants' gender was not included in the subsequent analysis as a moderator variable.

Hypothesis-Driven Analysis: Instagram Number of Posts and SDI

Means and standard error means of Instagram number of posts and SDI for *OXTR* rs53576 and *OXTR* rs2254298 are reported in Table 4.8.

As in the statistical plan of the study, Equation 4.1 was employed to test the existence of potential gene*environment interactions on Instagram number of posts and SDI. These hypothesis-driven analyses did not result in any main effect on the Instagram number of posts or SDI. Moreover, no interaction effect emerged between the SNP of interest (either *OXTR* rs53576 or *OXTR* rs2254298) and the two attachment dimensions (see Table 4.9).

***OXTR* rs53576**				
Number of Posts				
ECR-R dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.66 (0.07)	0.54 (0.05)	0.54 (0.07)	0.58 (0.07)
Avoidance	0.71 (0.08)	0.61 (0.06)	0.49 (0.04)	0.51 (0.06)
Social Desirability Index				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	-0.20 (0.05)	-0.04 (0.10)	-0.13 (0.04)	-0.26 (0.08)
Avoidance	-0.13 (0.04)	-0.12 (0.10)	-0.20 (0.04)	-0.20 (0.09)
***OXTR* rs2254298**				
Number of Posts				
ECR-R dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	0.60 (0.06)	0.56 (0.07)	0.59 (0.07)	0.54 (0.07)
Avoidance	0.67 (0.06)	0.61 (0.06)	0.52 (0.05)	0.49 (0.07)
Social Desirability Index				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	-0.14 (0.08)	-0.06 (0.10)	-0.22 (0.08)	-0.21 (0.06)
Avoidance	-0.14 (0.06)	-0.11 (0.11)	-0.23 (0.10)	-0.16 (0.04)

Table 4.8: Mean values in Oxytocin Receptor Gene (*OXTR*) rs53576 A/A homozygotes and G-carriers and Oxytocin Receptor Gene (*OXTR*) rs2254298 G/G homozygotes and A-carriers divided by Experience in Close Relationships-Revised (ECR-R) dimensions (high or low) on Instagram number of posts and Social Desirability Index, after removing the outlier values. Standard error means are reported between parentheses. Instagram behavior is reported by users' *OXTR* rs53576 phenotype and ECR-R dimensions, consistently with the literature on the topic and a previous publication (Bonassi et al., 2020b).

Exploratory Analysis: Instagram Number of Followings and Followers

Means and standard error means of Instagram number of followings and followers for *OXTR* rs53576 and *OXTR* rs2254298 are reported in Table 4.10.

From the performed ANCOVAs, a main effect of the *OXTR* rs53576 on the number of followings on Instagram was observed ($F(1,\ 53) = 5.78$, $p = 0.020$, p$\eta^2 = 0.11$). No other main effect of the two SNPs or ECR-R dimensions, and neither for their interplay, was observed on the Instagram variables (see Table 4.11.

OXTR rs53576					
Number of posts					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	0.0229	0.02292	0.429	0.5156
Anxiety	1	0.0131	0.01314	0.246	0.6223
Avoidance	1	0.1682	0.16820	3.147	0.0823
OXTR rs53576: Anxiety	1	0.2006	0.20064	3.754	0.0584
OXTR rs53576: Avoidance	1	0.0075	0.00749	0.140	0.7097
Residuals	49	2.6187	0.05344		
Social Desirability Index					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	0.000	0.00027	0.003	0.957
Anxiety	1	0.163	0.16284	1.772	0.189
Avoidance	1	0.012	0.01170	0.127	0.723
OXTR rs53576: Anxiety	1	0.108	0.10788	1.174	0.284
OXTR rs53576: Avoidance	1	0.000	0.00001	0.000	0.993
Residuals	49	4.504	0.09192		
OXTR rs2254298					
Number of posts					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.0284	0.02835	0.500	0.4828
Anxiety	1	0.0080	0.00804	0.142	0.7082
Avoidance	1	0.1834	0.18339	3.235	0.0782
OXTR rs2254298: Anxiety	1	0.0116	0.01157	0.204	0.6534
OXTR rs2254298: Avoidance	1	0.0221	0.02208	0.390	0.5354
Residuals	49	2.7777	0.05669		
Social Desirability Index					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.024	0.02375	0.261	0.612
Anxiety	1	0.155	0.15462	1.702	0.198
Avoidance	1	0.009	0.00856	0.094	0.760
OXTR rs2254298: Anxiety	1	0.033	0.03327	0.366	0.548
OXTR rs2254298: Avoidance	1	0.114	0.11382	1.253	0.269
Residuals	49	4.453	0.09087		

Table 4.9: Hypothesis-driven analysis: statistics' summary of ANCOVAs on Instagram number of posts and Social Desirability Index. For each Instagram variable considered in the hypothesis (Instagram number of posts and SDI) as dependent variable, one mixed ANCOVA was performed with *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates (see the top section of the Table). For each Instagram variable, one mixed ANCOVA was also performed with the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as a between-subject factor and the other parameters unchanged (see the below section of the Table).

***OXTR* rs53576**				
Number of Followings				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.53 (0.30)	-0.23 (0.19)	-0.08 (0.34)	-0.42 (0.15)
Avoidance	0.54 (0.31)	-0.20 (0.20)	-0.25 (0.28)	-0.44 (0.14)
Number of Followers				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.18 (0.14)	-0.16 (0.12)	-0.14 (0.16)	-0.26 (0.12)
Avoidance	0.13 (0.15)	-0.07 (0.14)	-0.07 (0.16)	-0.35 (0.07)
***OXTR* rs2254298**				
Number of Followings				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	-0.10 (0.23)	0.23 (0.27)	-0.40 (0.22)	-0.18 (0.23)
Avoidance	-0.07 (0.23)	0.37 (0.31)	-0.46 (0.21)	-0.31 (0.16
Number of Followers				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	-0.05 (0.13)	0.04 (0.14)	-0.20 (0.16)	-0.24 (0.10)
Avoidance	-0.03 (0.15)	0.08 (0.15)	-0.23 (0.14)	-0.28 (0.07)

Table 4.10: Mean values in Oxytocin Receptor Gene (*OXTR*) rs53576 A/A homozygotes and G-carriers and Oxytocin Receptor Gene (*OXTR*) rs2254298 G/G homozygotes and A-carriers divided by Experience in Close Relationships-Revised (ECR-R) dimensions (high or low) on Instagram number of followings and followers, after removing the outlier values. Standard error means are indicated between parentheses. Instagram behavior is reported by users' *OXTR* rs2254298 phenotype and ECR-R dimensions, consistently with the literature on the topic and a previous publication (Bonassi et al., 2020b).

OXTR rs53576					
Number of Followings					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	3.83	3.831	5.776	0.0202*
Anxiety	1	1.42	1.416	2.135	0.1505
Avoidance	1	2.40	2.398	3.617	0.0632
OXTR rs53576: Anxiety	1	1.03	1.034	1.560	0.2178
OXTR rs53576: Avoidance	1	0.13	0.130	0.197	0.6595
Residuals	48	31.83	0.663		
Number of Followers					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	0.835	0.8346	3.378	0.072
Anxiety	1	0.398	0.3981	1.611	0.210
Avoidance	1	0.398	0.3979	1.610	0.210
OXTR rs53576: Anxiety	1	0.168	0.1680	0.680	0.414
OXTR rs53576: Avoidance	1	0.139	0.1395	0.565	0.456
Residuals	50	12.354	0.2471		
OXTR rs2254298					
Number of Followings					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.91	0.906	1.273	0.2649
Anxiety	1	1.78	1.784	2.506	0.1200
Avoidance	1	3.51	3.507	4.928	0.0312
OXTR rs2254298: Anxiety	1	0.05	0.050	0.070	0.7920
OXTR rs2254298: Avoidance	1	0.23	0.234	0.329	0.5692
Residuals	48	34.16	0.712		
Number of Followers					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.003	0.0031	0.012	0.914
Anxiety	1	0.537	0.5369	2.040	0.159
Avoidance	1	0.534	0.5336	2.028	0.161
OXTR rs2254298: Anxiety	1	0.036	0.0362	0.138	0.712
OXTR rs2254298: Avoidance	1	0.026	0.0258	0.098	0.755
Residuals	50	13.156	0.2631		

Table 4.11: Exploratory analysis: statistics' summary of ANCOVAs on Instagram number of followings and number of followers. For each Instagram variable considered in the exploratory analysis (Instagram number of followings and followers) as dependent variable (DV), one mixed ANCOVA was performed with *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates, as in Equation 4.1 (see the top section of the Table). For each Instagram variable, one mixed ANCOVA was also performed with the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as a between-subject factor and the other parameters unchanged (see the below section of the Table). A significant main effects of the genotype was found on the number of followings for *OXTR* rs53576. (* $p < 0.025$).

As before, the direction of the observed effect was studied with a post-hoc two-tailed Student's t test. In particular, a significant difference between allelic groups (A/A vs. G alleles) on the number of followings was confirmed ($t = 2.33$, df = 52, $p = 0.024$, 95% CI [0.08, 1.03]; see Figure 10).

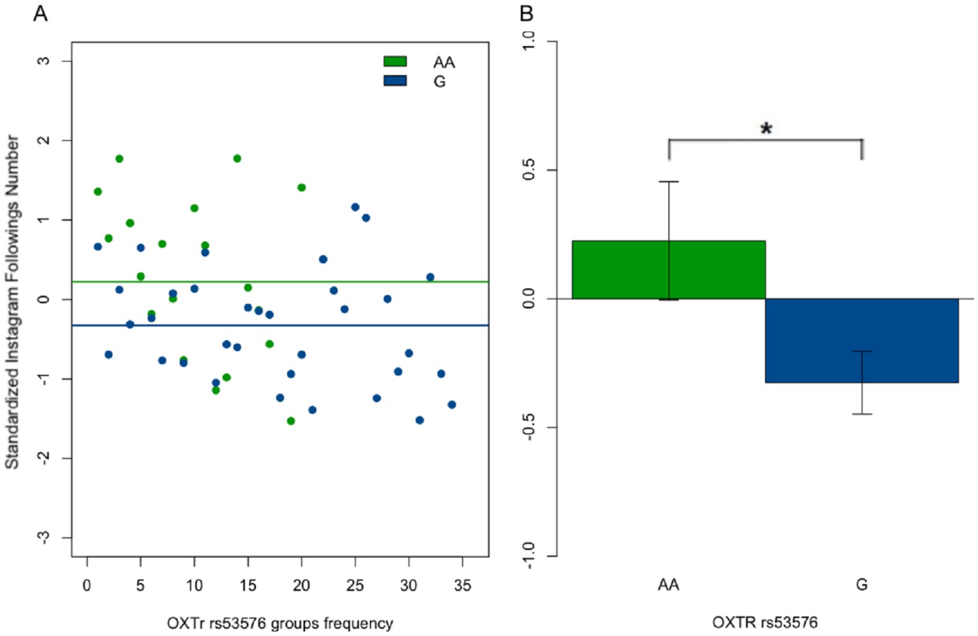

Figure 10: Main Effect of *OXTR* rs53576 on Instagram Number of Followings. On the left, effect of Oxytocin Receptor Gene (*OXTR*) rs53576 on the standardized Instagram number of followings. Green circles = A/A homozygotes; blue circles = G-carriers. Lines constitute the linear models for A/A homozygotes (green) and G-carriers (blue). On the right, comparison between the number of Instagram followings in A/A homozygotes (green) and G-carriers (blue) (* $p < 0.025$).

4.3.3 Results obtained replacing extreme values

Data were further explored through a third approach used to treat the outliers. In this case, the extreme values of each Instagram variable were replaced by the mean in observations excluding outliers. This method refers to the weight modification of the extreme values, allowing researchers to maintain a constant variability without reducing the sample size (Kwak and Kim, 2017; Van Selst and Jolicoeur, 1994).

Preliminary Analysis on the Genetic Variables

Table 4.12 reports the observed frequency of *OXTR* rs53576 and *OXTR* rs2254298 genotypes by the total sample size (for further details see Table S1 of the Supplementary Materials). In the context of *OXTR* rs53576, participants gender ($X^2(1) = 0.17$, ns) did not significantly differ between the two groups A/A vs G. As regards *OXTR* rs2254298, participants' gender ($X^2(1) = 0.81$, ns) did not significantly differ between the two groups G/G vs A.

OXTR rs53576	
Alleles	**Total**
AA	22 (38.60%)
AG	30 (52.63%)
GG	5 (8.77%)
G-carriers	35 (61.40%)
Total	57
OXTR rs2254298	
Alleles	**Total**
AA	4 (7.02%)
GA	21 (36.84%)
GG	32 (56.14%)
A-carriers	25 (43.86%)
Total	57

Table 4.12: Frequency values of the total Singaporean sample in Oxytocin Receptor Gene (*OXTR*) rs53576 and Oxytocin Receptor Gene (*OXTR*) rs2254298 genotypes. The frequency percentage of each genotype is reported between parenthesis. The presented allelic frequencies are consistent with the Hardy-Weinberg equilibrium (for *OXTR* rs53576, $X^2(1) = 1.376$, ns; for *OXTR* rs2254298, $X^2(1) = 0.047$, ns). The present data refer to the 57 participants which completed the entire assessment across three levels: genetic (*OXTR* rs53576; *OXTR* rs2254298), behavioral (Experience in Close Relationships-Revised questionnaire) and Instagram (number of posts, following, followers, and the Social Desirability Index) data collections.

Preliminary Analysis on ECR-R and Instagram Variables

Table 4.13 describes the values concerning the data distribution of each continuous variable (two ECR-R dimensions and four Instagram variables) in terms of skewness, kurtosis and descriptive statistics (see "Statistical Analysis" for further details).

To exclude any significant effect of participants' gender on Instagram variables, four preliminary two-tailed Student's t-tests were performed (corrected $\alpha = 0.0125$). As expected, no significant differences in the standardized Instagram number of posts ($t = 0.67$, df = 55, $p = 0.506$), followings ($t = 2.51$ df = 55, $p = 0.015$), followers ($t = 1.81$, df = 55, $p = 0.075$), and on the standardized SDI ($t = 0.89$, df = 55, $p = 0.377$) were found between male and female participants. This evidence allows to analyze data of female and male participants together in the subsequent

Variable	**Skewness**	**Kurtosis**	**Min**	**1st Q**	**Median**	**Mean**	**3rd Q**	**Max**	**SD**
Anxiety	-0.38	-0.02	1.39	3.33	3.94	3.94	4.56	6.22	1.08
Avoidance	-0.15	-0.39	1.06	2.11	2.94	2.95	3.67	5.39	0.93
Posts number	1.56	1.81	-0.60	-0.51	-0.36	-0.16	-0.02	1.36	0.49
Log-transformed posts number	1.14	0.43	0.33	0.40	0.49	0.58	0.68	1.21	0.23
Social Desirability Index	-0.70	2.75	-1.16	-0.27	-0.13	-0.16	-0.03	0.61	0.29
Followings	0.35	-0.62	-1.53	-0.77	-0.12	-0.12	0.51	1.78	0.85
Followers	0.78	0.16	-0.80	-0.50	-0.17	-0.11	0.22	1.45	0.51

Table 4.13: Summary of the descriptive statistics for each continuous variable. The distribution of each ECR-R (Experience in Close Relationships-Revised) dimension and Instagram variable is described in terms of Skewness, Kurtosis, Minimum (Min), first Quartile (1st Q), Median, Mean, third Quartile (3rd Q), Maximum (Max) and Standard Deviation (SD). Instagram variables were standardized using z-score transformation and inspected for normality. The eight values identified as outliers on Instagram variables were replaced by the mean in observations excluding outliers (see "Statistical Analysis" for further details). Skewness and kurtosis values were computed for each continuous subscale of the ECR-R questionnaire and each Instagram variable. Of all variables, only participants' number of posts did not follow the Gaussian distribution, and was thus adjusted by log-transformation. Log-transformed number of posts shows increased values compared to the original sampling of the same variable.

analysis.

Hypothesis-Driven Analysis: Instagram Number of Posts and SDI

Means and standard error means of Instagram number of posts and SDI for *OXTR* rs53576 and *OXTR* rs2254298 are reported in Table 4.14.

To detect potential gene*environment interactions on Instagram variables considered for the two hypotheses (number of posts, SDI values), two different mixed ANCOVAs were employed for each *OXTR* gene SNP: one ANCOVA with Instagram number of posts and one with Instagram SDI as DV for *OXTR* rs53576, whereas one ANCOVA with Instagram number of posts and one with Instagram SDI as DV for *OXTR* rs2254298. To take into account the increased possibility of committing a type I error, a false discovery rate correction was employed by means of a Bonferroni Correction (corrected $\alpha = 0.025$). Bonferroni's method for multiple testing correction was chosen rather than the available alternative ap-

***OXTR* rs53576**				
Number of Posts				
ECR-R dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.65 (0.07)	0.54 (0.06)	0.54 (0.06)	0.58 (0.07)
Avoidance	0.70 (0.07)	0.61 (0.06)	0.49 (0.04)	0.50 (0.06)
Social Desirability Index				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	-0.19 (0.05)	-0.05 (0.10)	-0.13 (0.04)	-0.26 (0.07)
Avoidance	-0.13 (0.04)	-0.10 (0.10)	-0.20 (0.04)	-0.19 (0.08)
***OXTR* rs2254298**				
Number of Posts				
ECR-R dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	0.61 (0.06)	0.56 (0.06)	0.59 (0.06)	0.54 (0.07)
Avoidance	0.65 (0.06)	0.64 (0.07)	0.52 (0.05)	0.48 (0.06)
Social Desirability Index				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	-0.15 (0.08)	-0.06 (0.10)	-0.21 (0.08)	-0.21 (0.06)
Avoidance	-0.14 (0.06)	-0.07 (0.12)	-0.22 (0.10)	-0.16 (0.04)

Table 4.14: Mean values in Oxytocin Receptor Gene (*OXTR*) rs53576 A/A homozygotes and G-carriers and Oxytocin Receptor Gene (*OXTR*) rs2254298 G/G homozygotes and A-carriers divided by Experience in Close Relationships-Revised (ECR-R) dimensions (high or low) on Instagram number of posts and Social Desirability Index. Standard error means are reported between parentheses. Instagram behavior is reported by users' *OXTR* rs53576 phenotype and ECR-R dimensions.

proaches to apply a more conservative correction.

A prior sensitivity power analysis conducted on GPower (power = 0.80) estimated that the analysis could detect a medium effect size (f = 0.42) via analysis of covariance given the current sample size (N = 57) and the corrected $\alpha = 0.025$ (ANCOVA: fixed effects, main effects and interactions).

In the analysis, *OXTR* rs53576 (A/A vs. G-carriers) and *OXTR* rs2254298 (G/G vs. A-carriers) were considered as separate predictors in distinct analyses. Two out of four mixed ANCOVAs included the *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates, as in Equation 4.1.

Likewise, the two remaining ANCOVAs included the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as the between-subject factor, and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates, as in Equation 4.1.

Results revealed no significant main effects of *OXTR* rs53576 ($p > 0.025$)

on Instagram number of posts and SDI. Moreover, no significant interactions between the ECR-R dimensions and *OXTR* rs53576 on Instagram number of posts and SDI were found (see Table 4.15).

Similarly, no significant main effects of *OXTR* rs2254298 or interaction effects between the ECR-R subscales and *OXTR* rs2254298 were obtained on the two Instagram variables.

Given that no significant effects from ANCOVAs were found, consequent post-hoc analyses were not implemented to test the directionality of the potential gene*environment interactions predicted by the hypotheses.

OXTR rs53576					
Number of posts					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	0.0246	0.02464	0.477	0.4929
Anxiety	1	0.0128	0.01277	0.247	0.6211
Avoidance	1	0.1499	0.14991	2.902	0.0945
OXTR rs53576: Anxiety	1	0.2077	0.20771	4.021	0.0502
OXTR rs53576: Avoidance	1	0.0037	0.00370	0.072	0.7901
Residuals	51	2.6341	0.05165		
Social Desirability Index					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	0.000	0.00027	0.003	0.956
Anxiety	1	0.162	0.16229	1.837	0.181
Avoidance	1	0.012	0.01204	0.136	0.714
OXTR rs53576: Anxiety	1	0.107	0.10749	1.217	0.275
OXTR rs53576: Avoidance	1	0.000	0.00001	0.000	0.990
Residuals	51	4.505	0.08833		
OXTR rs2254298					
Number of posts					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.0270	0.02700	0.492	0.4860
Anxiety	1	0.0074	0.00742	0.135	0.7145
Avoidance	1	0.1733	0.17326	3.160	0.0814
OXTR rs2254298: Anxiety	1	0.0076	0.00761	0.139	0.7111
OXTR rs2254298: Avoidance	1	0.0212	0.02116	0.386	0.5372
Residuals	51	2.7964	0.05483		
Social Desirability Index					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.023	0.02307	0.264	0.610
Anxiety	1	0.153	0.15316	1.753	0.191
Avoidance	1	0.009	0.00860	0.098	0.755
OXTR rs2254298: Anxiety	1	0.034	0.03402	0.389	0.535
OXTR rs2254298: Avoidance	1	0.112	0.11224	1.285	0.262
Residuals	51	4.456	0.08736		

Table 4.15: Hypothesis-driven analysis: statistics' summary of ANCOVAs on Instagram number of posts and Social Desirability Index. For each Instagram variable considered in the hypothesis (Instagram number of posts and SDI) as dependent variable, one mixed ANCOVA was performed with *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates (see the top section of the Table). For each Instagram variable, one mixed ANCOVA was also performed with the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as a between-subject factor and the other parameters unchanged (see the below section of the Table).

Exploratory Analysis: Instagram Number of Followings and Followers

Means and standard error means of Instagram number of followings and followers for *OXTR* rs53576 and *OXTR* rs2254298 are reported in Table 4.16.

***OXTR* rs53576**				
Number of Followings				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.42 (0.26)	-0.18 (0.20)	-0.08 (0.34)	-0.40 (0.14)
Avoidance	0.54 (0.31)	-0.25 (0.21)	-0.22 (0.22)	-0.44 (0.14)
Number of Followers				
ECR-R Dimension	**Low/AA**	**Low/G**	**High/AA**	**High/G**
Anxiety	0.18 (0.14)	-0.13 (0.12)	-0.14 (0.16)	-0.26 (0.12)
Avoidance	0.13 (0.15)	-0.06 (0.16)	-0.07 (0.16)	-0.34 (0.07)
***OXTR* rs2254298**				
Number of Followings				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	-0.04 (0.21)	0.23 (0.27)	-0.38 (0.21)	-0.18 (0.23)
Avoidance	-0.07 (0.23)	0.34 (0.33)	-0.41 (0.18)	-0.31 (0.16)
Number of Followers				
ECR-R Dimension	**Low/GG**	**Low/A**	**High/GG**	**High/A**
Anxiety	-0.02 (0.13)	0.04 (0.14)	-0.20 (0.16)	-0.24 (0.10)
Avoidance	-0.03 (0.16)	0.10 (0.17)	-0.22 (0.13)	-0.28 (0.07)

Table 4.16: Mean values in Oxytocin Receptor Gene (*OXTR*) rs53576 A/A homozygotes and G-carriers and Oxytocin Receptor Gene (*OXTR*) rs2254298 G/G homozygotes and A-carriers divided by Experience in Close Relationships-Revised (ECR-R) dimensions (high or low) on Instagram number of followings and followers. Standard error means are indicated between parentheses. Instagram behavior is reported by users' *OXTR* rs2254298 phenotype and ECR-R dimensions.

The hypothesis-driven approach adopted for Instagram number of posts and SDI was extended as exploratory analysis to the number of followings and followers. Therefore, a Bonferroni's correction was separately applied for the two exploratory tests (corrected $\alpha = 0.025$). To identify exploratory gene*environment interactions on two further Instagram variables that were collected (number of followings and followers), two mixed ANCOVAs were employed for each *OXTR* gene SNP: one ANCOVA with Instagram's number of followings and one with Instagram number of followers as DV for *OXTR* rs53576, whereas one ANCOVA with Instagram's number of followings and one with Instagram number of followers as DV for *OXTR* rs2254298. For each ANCOVA the between-subject factor and the covariates were unchanged, as in Equation 4.1. The ANCOVA performed on Instagram number of followings revealed a significant main effect of *OXTR* rs53576 genotype ($F(1,\ 56) = 5.71$, $p < 0.021$, p$\eta^2 = 0.10$), as indicated in Table 4.17. No further significant interactions between the ECR-R subscales and *OXTR* rs53576 on the Instagram number of followings were observed (see Table 4.17).

OXTR rs53576					
Number of Followings					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	3.57	3.571	5.706	0.0206*
Anxiety	1	1.21	1.213	1.938	0.1699
Avoidance	1	2.76	2.764	4.417	0.0405
OXTR rs53576: Anxiety	1	1.07	1.069	1.708	0.1971
OXTR rs53576: Avoidance	1	0.11	0.109	0.175	0.6779
Residuals	51	31.92	0.626		
Number of Followers					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs53576	1	0.825	0.8252	3.398	0.0711
Anxiety	1	0.400	0.4003	1.648	0.2050
Avoidance	1	0.382	0.3822	1.574	0.2154
OXTR rs53576: Anxiety	1	0.168	0.1683	0.693	0.4091
OXTR rs53576: Avoidance	1	0.129	0.1292	0.532	0.4691
Residuals	51	12.387	0.2429		
OXTR rs2254298					
Number of Followings					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.87	0.867	1.285	0.2623
Anxiety	1	1.62	1.617	2.398	0.1277
Avoidance	1	3.39	3.391	5.027	0.0293
OXTR rs2254298: Anxiety	1	0.06	0.059	0.087	0.7689
OXTR rs2254298: Avoidance	1	0.31	0.312	0.463	0.4993
Residuals	51	34.40	0.674		
Number of Followers					
Variable	**DF**	**Sum Square**	**Mean Square**	***F* value**	***p*-value**
OXTR rs2254298	1	0.003	0.0030	0.012	0.914
Anxiety	1	0.537	0.5369	2.081	0.155
Avoidance	1	0.527	0.5271	2.042	0.159
OXTR rs2254298: Anxiety	1	0.036	0.0360	0.140	0.710
OXTR rs2254298: Avoidance	1	0.028	0.0278	0.108	0.744
Residuals	51	13.161	0.2581		

Table 4.17: Exploratory analysis: statistics' summary of ANCOVAs on Instagram number of followings and number of followers. For each Instagram variable considered in the exploratory analysis (Instagram number of followings and followers) as dependent variable (DV), one mixed ANCOVA was performed with *OXTR* gene genotype rs53576 (A/A and G-carriers) as a between-subject factor and the ECR-R dimensions (Anxiety and Avoidance) as continuous covariates, as in Equation 4.1 (see the top section of the Table). For each Instagram variable, one mixed ANCOVA was also performed with the *OXTR* gene genotype rs2254298 (G/G and A-carriers) as a between-subject factor and the other parameters unchanged (see the below section of the Table). A significant main effects of the genotype was found on the number of followings. (* $p < 0.025$).

To explore the direction of the ANCOVA effect, a further post-hoc two-tailed StudentâĂŹs t test was computed. The Student's t test confirmed that the number of Instagram followings was significantly different between the A/A vs G allele groups ($t = 2.30$, df $= 55$, $p < 0.025$, $d < 0.63$) (see Figure 11).

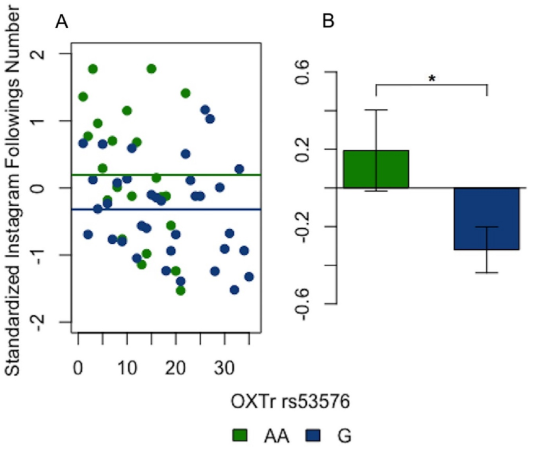

Figure 11: Main Effect of *OXTR* rs53576 on Instagram Number of Followings. (**A**) Effect of Oxytocin Receptor Gene (*OXTR*) rs53576 on the standardized Instagram number of followings. Green circles = A/A homozygotes; blue circles = G-carriers. Lines constitute the linear models for A/A homozygotes (green) and G-carriers (blue). (**B**) Comparison between the number of Instagram followings in A/A homozygotes (green) and G-carriers (blue) (* $p < 0.025$).

No significant main effects of *OXTR* rs53576 or interaction effects between the ECR-R dimensions and *OXTR* rs53576 were found on Instagram number of followers ($p > 0.025$), as reported in Table 4.17. With regards to *OXTR* rs2254298, no significant main effects of genotype or interaction effects between the ECR-R subscales and genotype were identified on Instagram number of followings, as reported in Table 4.17. Likewise, no significant main effects of *OXTR* rs2254298 or interaction effects between the ECR-R dimensions and *OXTR* rs2254298 were identified on Instagram number of followers (see Table 4.17).

4.4 Discussion

For the more rigorous analyses applied, the discussion will focus on the results obtained excluding outliers.

Two gene*environment interactions on the number of posts and SDI (*OXTR* rs53576 SNP * close relationship in adulthood; *OXTR* rs2254298 SNP * close relationship in adulthood) were initially hypothesized.

Contrary to these predictions (see the chapter 5 for an extensive overview on the expected patterns and the obtained results), only a main effect of gene *OXTR* rs53576 on Instagram number of followings was found. Post-hoc tests revealed differential Instagram behavior between the two genetic groups within the *OXTR* rs53576. Independent of the reported scores on anxiety and avoidance in adult relationships, A/A homozygotes showed a higher number of followings compared to G-carriers. Previous researches highlighted that *OXTR* rs53576 G allele is linked to higher marital satisfaction, support seeking in hostile circumstances, and higher empathy than A-carriers (Gong et al., 2017; Monin et al., 2019). Conversely, in a few cases, A/A individuals were found to display increased social attitudes and higher social sensitivity than G-carriers (Zheng et al., 2020). On the other hand, the G allele of the *OXTR* rs2254298 has been associated with separation anxiety, depression, decreased online sociability and lower reciprocity in a support-giving interaction (Costa et al., 2009; Schneiderman et al., 2014; Bonassi et al., 2020c). Overall, the role played by the A and G alleles on the *OXTR* SNPs towards general social behavior is debated (Kim et al., 2010). This debate will be clearer if the genetic correlates of social media behavior were investigated.

In connection to the findings of the study, distinct biological roots could have differently shaped online behavior among genetic groups (i.e. *OXTR* rs53576 A/A versus G-carriers), specifically the level of online sociability on SNSs, like Instagram. A high number of followings could represent the desire of Instagram's user to be involved in social interactions (Sherlock and Wagstaff, 2019; Bonassi et al., 2020c). Specifically, A/A homozygotes could exhibit a genetically-founded inclination to online sociability witnessed by a higher frequency of online behaviors (i.e. Instagram number of followings) than G-carriers. As a protective factor (Laursen et al., 2014; Smearman et al., 2015), A allele could predispose the user to be less anxious in online prosocial activities and proactively seek contact with other Instagram users. In contrast, G allele could predispose the user to be less interested or less motivated to search for others on Instagram. Given the contradictory results from the literature on the alleles of *OXTR* rs53576 (Bethlehem et al., 2014; Andreou et al., 2018; Cataldo et al., 2018a), it is open to question which allele is the bearer of a detrimental effect. However, in light of the Differential Susceptibility model (Belsky and Pluess, 2009a), we assumed that the genetic properties related to a given allele could not wholly determine online sociability only in terms of the "positive" (protective factor) versus "negative" (risk factor) predisposition (Roisman et al., 2012). Rather, every individual could exhibit a range of virtual social behaviors as a function of the interaction between genetic sensitivity to experiences, and environmental influences (Belsky et al., 2007; Ellis and Boyce, 2008). Within this framework, the current results suggest that no interaction between the quality of close adult relationships and the genetic predispositions for *OXTR* rs53576 or *OXTR* rs2254298 could explain Instagram sociability under a gene*environment perspective. This outcome finds agreement with previous research which did not identify an association between the *OXTR* rs53576 and close relationship main dimensions (Li et al., 2015; Gillath et al., 2008). In conclusion, multiple environmental components (i.e. quality of relationships with people) and genetic factors (i.e., *OXTR* rs53576 or *OXTR* rs2254298) could differently modulate users' online prosociality and frequency of virtual interactions (i.e. high number of followings). Since no interaction effect between genotype and close relationships was found, here, *OXTR* rs53576 could shape the level of Instagram sociability independent of the potential influence of the close adult relationship with one's partner. The current findings could inspire future research in exploring online sociability under a gene-environment perspective.

Chapter 5

General discussion and future directions

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[0] Chapter partly based on the following preregistered and published studies:

Study 1. Cataldo, I., Bonassi, A., Lepri, B., Foo, J. N., Setoh, P., Esposito, G. (2021). Recalled parental bonding interacts with oxytocin receptor gene polymorphism in modulating anxiety and avoidance in adult relationships. *Brain sciences*, 11(4), 496. DOI: 10.3390/brainsci11040496.

Study 2. Bonassi, A., Cataldo, I., Gabrieli, G., Foo, J. N., Lepri, B., Esposito, G. (2020). Oxytocin receptor gene polymorphisms and early parental bonding interact in shaping Instagram social behavior. *International journal of environmental research and public health*, 17(19), 7232. DOI: 10.3390/ijerph17197232.

Study 3. Carollo, A., Bonassi, A., Cataldo, I., Gabrieli, G., Tandiono, M., Foo, J. N., Lepri B., Esposito, G. (2021). The relation between Oxytocin Receptor Gene polymorphisms, adult attachment and Instagram sociability: An exploratory analysis. *Heliyon*, 7(9), e07894. DOI: 10.1016/j.heliyon.2021.e07894.

The general discussion links the studies presented in the previous chapters (studies 1, 2, 3) and those not reported (studies labelled as A, B, C, D, E, F) of the research project into a unique framework.

5.1 Theoretical discussion and clinical implications

5.1.1 The research project: a general overview

Across several project studies, sociability was examined as the primary outcome at the intersection of multiple factors. Affiliative and social behaviours are evolutionarily driven to support cooperation with conspecifics (e.g., care, reproduction) and adaptation to the context (e.g., protection) (Jaeggi et al., 2010), thus safeguarding the survival from environmental hazards (Lehmann and Rousset, 2010) and increasing the sense of inclusiveness (Brosnan and Bshary, 2010).

Research in developmental psychobiology tried to unveil the complex nature of the social mind and behaviour, characterized by typical and atypical traits. Social traits can be the same (continuous and stable) or change over time, singularly or in tune with other traits. Patterns of consistency (vs change) over time describe the continuity (vs discontinuity) and the stability (vs instability) of social development along peculiar trajectories (Bornstein et al., 2017). Numerous elements can mitigate such trajectories. A large body of evidence highlighted the impact of the quality in caregiver-infant interactions on the developmental trajectories (Callaghan and Tottenham, 2016; Doyle and Cicchetti, 2017). In the current studies, early caregiving has been granted a pivotal role in social development. Sensitive parents respond promptly to infants' needs or requests and promote confidence towards others and autonomy in play and motor activities. Attachment (secure vs insecure) has short and long term consequences. In the short term, children reproduce social conducts, and stress responses are absorbed in the early caregiving environment (McLaughlin et al., 2015). In the long term, caregiving experiences predict child and adolescent brain development with long-lasting effects on physiology and social behaviour (Kok et al., 2015). Adult psychopathology and atypical social attitudes are traced back to stressful early life and adverse caregiving (LeMoult et al., 2020). An empathetic relationship with friends (adult attachment) or a trustworthy relationship with the partner (romantic attachment) instead lead back to previous positive parent-infant interactions (secure infant attachment) (Zayas et al., 2011). Inter-generational transmission of caregiving is also genetically explained (Bos, 2017). However, caregiving propensities towards the child in the early environment cannot represent the unique socio-emotional development factor. At an ontogenetic level, cultural factors regulate the social life outside the family and influence caregivers' mindset (Tajima and Harachi, 2010). At a phylogenetic level, genetic factors (e.g., OXTR, 5-HTTLPR) predispose the social brain (the phenotype) to express specific traits which affect the physiological and behavioural responses towards social cues (Truzzi et al., 2017, 2018; Cataldo et al., 2020). Overall, adult social attitudes may result from the dynamic unfolding of early caregiving, genetics, and culture. The current research project tried to understand the weight of each factor and the way these factors interact in modulating in-person (e.g., studies 1, and further A, B, C) and online social attitudes (e.g., study 2, and D). Although all these works looked at parental bonding as an environmental factor (measured by the PBI), only study 1 included the variable culture. Both studies 1 and 2 considered OXTR rs53576 and rs2254298 as genetic region(s), while study A focused on 5-HTTLPR, and further studies B, C, D on 5-HT rs25531. Furthermore, this project investigated the effect of quality in adult relationships (both among peers and spouses) on online social behaviour (study 3, and further D, E, F). Adult attachment (relationships with peers) and romantic attachment (close relationship) were respectively measured by the Adult Style Questionnaire (studies C and F) and the ECR-R (studies 1, 3, and further A, B). Instagram social patterns were considered as a proxy of online social interactions (study 2, 3 and further D, E, F).

The present investigations proved to be observational and exploratory. Firstly, they directly measured the variables of interest and observed how data were related without manipulation. Secondly, they probed the effects emerging from the complex interactions of the measured variables merging the contributions of developmental psychology, behavioural genetics, social neuroscience and computer science. To summarize, every study examined different shades of the complex portray of social behaviour.

5.1.2 Study 1: early caregiving interacts with cultural and genetic factors in moderating adult attachment and in-person social attitudes

This study aimed to scrutinise the effects of the genetic susceptibility of *OXTR* and early parental bonding on the levels of anxiety and avoidance experienced in romantic relationships in two different cultural contexts, namely Italy (Western-oriented) and Singapore (Eastern-oriented). In the current approach, the different combinations of the single variants for the Italian and Singaporean groups were divided to maximise the genetic distribution effects in the different ethnic groups. Results revealed main effects, two-way and three-way interaction effects at increasing levels of complexity tested via hierarchical linear modelling on the Italian, Singaporean, and the total sample. With regards to the Western-oriented culture, higher levels of experienced maternal control in childhood predicted higher anxiety scores towards the partner in adulthood (Ispa et al., 2004). From a clinical perspective, stress and anxiety exacerbate maternal overprotection, which interferes with the mother-infant attachment and generates further long term anxiety in the child. Maternal avoidance in play, as well as a decrease in the dyadic mutuality, represent a child's compensatory strategy which may persist until adulthood (Zdebik et al., 2018; Cooke et al., 2019). Regarding the Eastern-oriented culture, maternal care significantly affected avoidance scores in close adult relationships with a negative slope. Moreover, the interaction between *OXTR* polymorphisms and maternal care predicted adult avoidance. There was a negative association between maternal care and avoidance for A/A homozygotes instead of the positive association between the same dimensions for G-carriers. This differential pattern was expected from previous research (Bonassi et al., 2017; Truzzi et al., 2018; Senese et al., 2019). Emotional neglect in childhood is related to lower oxytocin levels in the plasma, which, in turn, lead to insecure attachment and high avoidance in social situations (Müller et al., 2019) until adulthood (Ein-Dor et al., 2018). When the analyses were conducted on the total sample, the effect of early maternal overprotection, as well as interaction effects among maternal caregiving and culture and *OXTR*, were highlighted. Here, the less frequent genetic variant for each population (A/A for the Italian sample, G/G for the Singaporean group) was more sensitive to early maternal overprotection, displaying greater levels of avoidance. This outcome supports the pattern found by Kim et al. (2010) on a Western-oriented culture: G-carriers reported seeking more emotional support than A/A homozygotes in conditions of high psychological distress, whereas they reported seeking less emotional support than A/A homozygotes in conditions of low psychological distress. Thus, Western individuals with genotype G/G may be greater in positive emotional expressivity as well as in seeking emotional support as an effect of culture on genetic predispositions (Ishii et al., 2021). In contrast, A/A may be associated with a higher tendency to emotional suppression due to avoidant attachment. A potential explanation could be genetically inferred: higher *OXTR* methylation and lower oxytocin levels in the plasma are associated with insecure attachment in young adulthood (Ebner et al., 2019). Differently from previous works, which found inconsistent results on the Eastern sample (Kim et al., 2010), the current study underlines the differential avoidant response among genotype of Western and Eastern individuals as a function of caregiving history.

Beyond the genotype *OXTR* rs53576, which is generally investigated in association with sociality (Li et al., 2015), two different social environments were compared: the family, within which the person experiences early relationships and builds the first behavioural patterns, and the cultural context, in which the grown person adopts a combined set of individual and shared criteria in relating to others. One of the strengths of this study is to provide a further step in comparing two distinct environments, each consisting of parenting strategies and family composition. Another critical element considered was the distinction between maternal and paternal bonding. While competence regarding childcare is becoming more and more equal between the two parents, fatherhood is an area that is still under-explored, especially regarding the temporal dynamics of attachment in adulthood. Avoidance might have been more strongly correlated as it could play a mediating role between recalled parental features and anxiety (Fulton et al., 2014). Overall, this study represents a further step in the modulation of the expectations and representations for close in-person relationships by early parental bonding, cultural belonging, and predispositions from the *OXTR*. The implications of these findings for clinical work could cover an expanding area of interest in line with the current biopsychosocial model of health and psychological wellness, the influence of cultural components and early interactions in understanding the development of social behaviour and related disorders. This would allow practitioners in child development and parenting fields to formulate interventions that also consider the cultural features of the person, which is a relevant topic due to the increasing mobility of single people and families.

5.1.3 Study 2: early caregiving interacts with genetic factors in moderating online social attitudes

The purpose of this study was to inspect the effects of the genetic susceptibility of *OXTR* and early parental bonding on the levels of online sociability in a cultural context highly sensitive to smart technologies, such as Singapore. The hypothesis-driven analysis predicted differential gene-by-environment interactions on the number of posts and followings on Instagram as the main parameters of online prosociality. Conversely, exploratory analyses applied the same statistical plan on the Instagram number of followers and the novel SDI. Regression analyses disclosed the main effects of early caregiving and two-way and interaction effects on the Instagram variables. The interplay between paternal care and *OXTR* rs2254298 affected the Instagram number of posts of Singaporean users. The higher paternal care experienced in childhood, the greater the number of published posts in adult users genetically sensitive to early environmental influences (e.g. rs2254298 G/A or A/A). At an exploratory level, the SDI of these users was predicted by the recalled maternal overprotection and the same genotype. The importance of caregiving practices was again confirmed for A-carriers: the higher the maternal control perceived at an early age, the higher the SDI value, which means that such users are inclined to build an enlarged social network to maximize the approval that they can receive from other users. This tendency may explain one of the purposes of Instagrammers who want to succeed and become influential (e.g., as an influencer). These observations are in line with previous works which found that Singaporean adolescents adjust Instagram browsing, posting, and editing as a function of peer appearance comparisons (Chang et al., 2019). Research emphasizes the negative role of social comparison in SNSs as Instagram, which mediates the pathway to higher social anxiety and lower body self-esteem (Tiggemann et al., 2018; Jiang and Ngien, 2020). However, research has not yet investigated the dynamics of Instagram behaviour as a function of caregiving behaviours in a sample of Singaporean users. Much could also depend on the motivation which inspires users in Instagram photo-sharing. Comparison processes in online (and offline) social behaviour can elicit a positive emotional response towards other users (e.g., benign envy) (Meier and Schäfer, 2018). From a genetic perspective, overall A-carriers but not G/G homozygotes exhibited weakened social responses on Instagram when they reported negative scores of interactions with their caregiver in childhood.

In contrast, the genotype rs2254298 G/G protective factor made users less susceptible to positive and negative caregiving. Differently from study 1, the hypothesis of the present study that *OXTR* rs53576 would moderate the action of parental bonding on social behaviour was null. However, a considerable difference should be kept in mind: the effect of *OXTR* rs53576 could be evident on adult attachment for in-person social relationships, but not for online social attitudes and behaviour as on Instagram. This divergence could open an intriguing debate (less or more speculative) on the genetic regions respectively involved in offline and online social competence. Methodological reasons could explain why *OXTR* rs53576 did not produce the expected results pointing to potential biases (see the section "Limitations, Conclusions and Future Directions").

Overall, this study represents a first attempt at the impact of early parental bonding and *OXTR* predispositions on Instagram social attitudes. To this day, no other studies have analysed Instagram activity from a gene-by-environment perspective. The role played by genes related to early-environment exposure during infant-parent interaction on the online social relationships is considerably recent and underexplored (Miller et al., 2012; Deryakulu and Ursavaş, 2014; York, 2017). Specifically, the present research examined Instagram behaviour, a novel area to be explored, on a non-Western sample, which is usually underrepresented in psychological studies (Nielsen et al., 2017a). This study proposed the SDI as a balanced and straightforward measure to evaluate the symmetry of a social network like Instagram. This index could help cluster different user groups and distribute the scoring along a continuum from a minimum to a maximum number of followers over followings. Users who are not skilled with Instagram services will show a limited number of followers, while more competent users with good quality content will get higher follow back rates. Interestingly, Instagram posting activity and the SDI results could be strongly linked parameters since the former could characterize the first means to enhance the latter.

From an educational perspective, a relationship promoting dialogue between parents and kids could represent a valuable resource in guiding social behaviour towards peers (Laible, 2007) and supervising Internet and social media usage (Yates et al., 2012). A trusting but not excessively controlling presence of the parents may allow increasing the autonomy of the child in managing social media content (Lee and Chae, 2007). A moderating action of parents in the administration of online life (e.g., defining a maximum duration of use, watching digital content with parents, discussing and clarifying the visualized content with parents) can train their child's ability to recognize the potential risks of the web (Kirwil, 2009) and reduce the risks of developing addiction associated with the problematic use of the Internet and online services (e.g., Internet use disorder, Internet gaming disorder, Hikikomori syndrome) (van Den Eijnden et al., 2010; Teo and Gaw, 2010; Paulus et al., 2018), such as social media (Hawk et al., 2019; Marino et al., 2020).

5.1.4 Study 3: adult attachment interacts with genetic factors in moderating online social attitudes

The objective of this study was to explore the effects of the genetic susceptibility of *OXTR* and anxiety and avoidance experienced in romantic relationships on the levels of online sociability. The experimental design of study 2 was applied to study 3 with variations in the collected data. Here, attachment in close relationships was considered a mediator intertwined with the genetic factor to determine whether this variable could impact online social attitudes. Previous research showed that dissatisfaction in the relationship with the spouse is linked to social media addiction (Demircioğlu and Köse, 2018). With regards to Instagram, posts on body image satisfaction from a partner may elicit romantic negative relationship (Ridgway and Clayton, 2016). In the context of online interactions, no works about the interplay of genes and adult attachment on social media behaviour were carried out to date. In the context of in-person interactions, *OXTR* SNPs effects associated with adult attachment and general sociability are still matter of debate (Rodrigues et al., 2009; Bakermans-Kranenburg and van IJzendoorn, 2008; Yamasue, 2013; Lee Raby et al., 2013a; Bakermans-Kranenburg and Van Ijzendoorn, 2014; Li et al., 2015; Pearce et al., 2017; Gong et al., 2020). Starting from the significant evidence of study 2, hypothesis-driven analysis of the current study predicted differential gene-by-environment interactions on the Instagram number of posts and SDI. Exploratory analyses still implemented the same statistics on the Instagram number of followings and followers. Multiple mixed ANCOVAs have been employed to test the hypothesis. Differently from study 2, analyses were separately performed on unaltered data (outliers were maintained in the data distributions), cleaned data (outliers were removed) and altered data (the mean in observations excluding outliers replaced outliers) and their results were compared. This methodological approach emphasised how diverse statistical plans may alter data observations with repercussions on the results. Findings from the most conservative and rigorous method (excluding outliers) are discussed. Contrary to expectations, no significant interaction effects were found on the hypothesis-related variables. Exploratory analysis revealed a main effect of the gene *OXTR* rs53576 on Instagram number of followings. Within the *OXTR* rs53576, post-hoc tests confirmed a significant difference in Instagram behaviour between A/A and G-carriers. Independent of the anxiety and avoidance felt towards the partner, A/A homozygotes showed a higher number of followings than G-carriers. As study 1 and opposed to study 2, *OXTR* rs53576 but not *OXTR* rs2254298 had a direct influence on Instagram sociability. The discrepancy between the expected patterns and the obtained results at a genetic level require some consideration. For instance, an absolute consensus on the predisposition given by *OXTR*/rs53576 A or G allele does not exist (McQuaid et al., 2013) and the culture-dependent variation of allelic distributions should not be ignored (Sasaki et al., 2011). Nonetheless, no interaction effect was detected between genes and close relationship scores. This finding is confirmed by previous research, which highlighted no associations between *OXTR* and adult attachment (Lee Raby et al., 2013a; Gong et al., 2020). Data interpretation is even more challenging in the presence of a genetic influence independent of the environmental exposure (Lee et al., 2003; Bugental and Grusec, 2007) on an underexplored social variable such as Instagram number of followings. Although there is no firm evidence of gene-environment interactions on online sociability, the existing literature on general or in-person sociability or emotional support reveals that multiple factors could determine the role that A or G alleles play in the individuals' lives (Luo and Han, 2014). In conclusion, this study represents an exploratory attempt to unmask a potential influence of romantic relationships and *OXTR* predispositions on Instagram social attitudes.

5.1.5 The biggest picture: the proposal of a theoretical model on social behaviour

The ultimate goal of the research project was to detect the main predictors of social behaviour[1]. The influence of three significant factors was detected by combining the findings obtained from the three studies.

Firstly, early caregiving propensities shape social development from childhood to adulthood with effects on adult relationships, both in-person with the partner (study 1 - (Cataldo et al., 2021a); study A - (Bonassi et al., 2021b); study B - (Bonassi et al., 2021c)) or peers (study C - (Bonassi et al., 2021d)) and online with other users (study 2 - (Bonassi et al., 2020b), study D - (Bonassi et al., 2020c)). Based on their outcomes, Study 1 and 2 meet the postulate of the Prototype Hypothesis. As suggested by study 1, adult attachment representations echo those formed in infancy: the partner replaces the role of early caregiver with a comparable function of social regulation. Study 2 highlights that posi-

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[1] In the present subsection all the studies of the research project are cited within the text and labelled by number (the main studies 1, 2, 3) or letter (the secondary studies A, B, C, D, E, F).

tive caregiving practices may enhance social and prosocial conduct, even online (e.g., Instagram stories or posts). Interestingly, high quality in parent-infant interactions may support the involvement in social communities and the creation of new contacts in the social network (e.g. Instagram followers).

Secondly, genotype plays a pivotal role in moderating social propensities towards the partner (study 1) and the users (studies 2 and 3). Every study satisfies the assumptions of the Differential-Susceptibility and Resilience Hypothesis. In particular, the findings show how *OXTR* modulate the flexibility of offline (study 1) and online sociability (studies 2 and 3). In general, humans whose DNA codes for fixed social attitudes will develop similarly, less affected by parental behaviour. In contrast, humans whose DNA codes for malleable social attitudes will develop according to the quality of the caregiving experiences, either positive or negative. Plastic (e.g., the Italian A/A and the Singaporean G/G for rs53576 in study 1; the Singaporean A/A for rs2254298 in study 2) and non-plastic (e.g., the Italian G/G and the Singaporean A/A for rs53576 in study 1; the Singaporean G/G for rs2254298 in study 2) genotypes favour social development and increase survival in two ways. In the plastic scenario, higher social flexibility enhances adaptation and heightens social development in a favourable early environment. In the non-plastic scenario, steady behavioural and physiological patterns of sociability intensify resilience and inhibit maladaptive outcomes in an adverse early environment.

Thirdly, culture leaves the print on environment and genotype. In the first case, community and societal norms implicitly direct individual habits and mindset, from caregiving practices to daily social behaviour. In the second case, genotypes' distributions vary according to the ethnic origin of a given population. For this reason, the alleles' frequency (e.g., A/A versus G/A versus G/G) of the Italian population can be so different from that of the Singaporean population within the same genetic region (e.g., *OXTR* rs2254298).

A fourth potential predictor of adult social behaviour could be the offline relationship with the partner. This component has not been included since findings are controversial. Within this project, Study 3 (Carollo et al., 2021a) did not capture any potential prediction of quality in close relationships on Instagram social attitudes when *OXTR* SNPs were considered. In parallel, study E (Bonassi et al., 2021a) identifies an effect of adult attachment on Instagram social behaviour when *5-HT* rs25531 was taken as a genetic factor.

A fifth potential predictor of adult social behaviour could be the offline relationship with friends. None of the studies described in the previous chapters tested this hypothesis. Other preliminary studies of the project did not find correspondences between attachment with peers and *OXTR* on Instagram social attitudes. Study F (Bonassi et al., 2020a) instead highlighted a link between the relationship with peers and *5-HT* rs25531 on the frequency in the online sociability of users.

Overall, the research project embodies the Bioecological Model of development, which proposes an all-embracing view of social development, shaped by the inter-relations between genes, environments and culture at different degrees (Bronfenbrenner and Ceci, 1994). Genotype firstly outlines the developmental trajectory, which will undergo several corrections from numerous factors. Among a variety of environmental factors, relationships with family and peers and religious teaching have a first direct effect on child development (Bronfenbrenner, 1995). In the second rank, the local community, school system, media environment, and health services affect children's beliefs and behaviours (Bronfenbrenner, 1999). In the final rank, cultural values, social conditions and socioeconomic status indirectly modulate social attitudes. Ecological theorists prompt the need for different methodologies (e.g., the Attachment Theory, Behaviourism and Piaget's Theory of Cognitive and Intellectual Development) to understand the interactions between such factors. The basis of the Attachment Theory combined with the theoretical foundations of behavioural genetics and modern cyberpsychology is here applied to investigate the effects of the interaction among *OXTR* and *5-HT* genes, culture and early or adult social relationships on the levels of sociability. In light of the overview of the research project, a theoretical model is advanced to integrate the numerous factors into a unique and coherent framework. The model is depicted in Figure 12 and represents the set of predictors of social behaviour.

Firstly, nature (genetic and biological properties) and culture are reported as fixed factors. The term “fixed” here denotes a set of planned and “prearranged” factors whose iterative effects on development are immediate since maternal pregnancy and last for the whole life. Culture (Figure 12A) accounts for the immersive world of norms, laws, customs, traditions, beliefs, and behaviours that surround humans from birth. Variations within a given culture are possible but require a long time to change at a societal level. Ethnicity (here included in the construct “culture”) also constraints genotype, specifically the frequency in allele distributions. DNA (Figure 12B) refers to hereditary material and traits genetically determined. Epigenome (here part of the construct “Genome”) controls genome expression through complex chemical compounds, instead reversible and subject to change. It is therefore clear that culture and genetics are not exempt to potential modifications. Rather, their mutations are complex and triggered by environmental conditions. Effect of gene-by culture interactions act throughout the course of development (Figure 12: $A \times B \to C, D, E, F$).

Parent-infant relationship (Figure 12 C) embodies the first social interaction and the parent is a “secure base”. Early attachment regulates a child’s behaviour and adjusts the longitudinal trajectory of social development. As evidence, Esposito et al. (2017e) reported that individuals with a genetic vulnerability (*OXTR* rs2254298 A-carriers) and a history of high paternal overprotection showed an increase in heart rate and a decrease in nose temperature to social distress than those with the protective factor (G/G genotype). Caregiving intertwined with cultural and genetic factors display effects on in-person social behaviours, such as peer relationship (Figure 12: $A \times B \times C \rightarrow D$) and relationship with the partner (Figure: 12 $A \times B \times C \rightarrow E$).

In the context of peer relationships (Figure 12 D), a NIRS study (study C - (Bonassi et al., 2021d)) highlighted different oxygenated haemoglobin concentrations in the prefrontal cortex to stressors between Singaporean participants with genotypes of differential susceptibility (*5-HT* rs25531 T/T vs C group) when they thought that their relationships with peers were secondary (avoidance). In the context of close relationships (Figure 12 E), study 1 (Cataldo et al., 2021a) mostly confirmed the long-term impact of gene-by-culture interactions and maternal caregiving on the quality of the relationship with the partner across Italy and Singapore. In line with the findings of study 1, study A (Bonassi et al., 2021b) verified that *5-HTTLPR* and recalled maternal overprotection predicted avoidance in romantic relationships in Italy. Moreover, both adult anxiety and avoidance were found to covary as a function of averse motherhood. Similarly, study B (Bonassi et al., 2021c) indicated that Singaporean individuals with the cytosine variation (gene *5-HT* rs25531) who recalled a past of paternal overprotection displayed a higher tendency of avoidance from the intimate partner. These results suggest that motherhood and fatherhood have a crucial role in child development, whose quality outlines long-term effects throughout life experiences.

In addition to the cultural and genetic factors, early caregiving has significant effects on in-person social behaviours as well, such as user-to-user relationships on SNSs (Figure 12: $A \times B \times C \rightarrow F$). Study 2 (Bonassi et al., 2020b) firstly provides an insight into the mediation of *OXTR* and levels of parental bonding on Instagram number of posts and SDI of Singaporean users. In line with the outcome of Study 2, Study D (Bonassi et al., 2020c) validated the prediction of *5-HT* rs25531 and early maternal care on SDI values. In comparison with the patterns of Study B and C on in-person social behaviour and attachment, study D focusing on online sociability, revealed that T/T homozygotes scored higher SDI points than C-carriers when positive maternal care was experienced.

Within a feedback circuit, peer and close relationships are not merely the final stages of development, but, in turn, rule adult in-person and online social behaviour (Figure 12: $C + D \rightarrow F$). As discussed, Study 3 (Carollo et al., 2021a) mainly outlined the dominant contribution of *OXTR* rs53576 over the expectations in the close relationship on the number of Instagram followings of Singaporean users. In contrast, Study E (Bonassi et al., 2021a) pointed out the leading role of adult attachment over the *5-HT* rs25531 effect. Here, avoidance from the partner was a linear predictor of the Instagram number of followings with positive evidence estimated by the Bayesian information criterion index. In line with the findings of study D, study F (Bonassi et al., 2020a) observed that Singaporean users with the genotype more sensitive to environmental influences (*5-HT* rs25531 T/T) had a greater Instagram number of followings than non-sensitive ones (C-carriers) when they admitted a high level of confidence towards others (offline).

In turn, online social behaviour (Figure 12 F) regulates adult social propensities towards others in the offline environment, as witnessed by research in the field (Demircioğlu and Köse, 2018; Nowland et al., 2018; Stockdale and Coyne, 2020) (Figure 12: $F \rightarrow C + D$). The overall results on social media behaviour support the Complementary Hypothesis (MacDonald and Schermer, 2021) which states that social patterns of both online and in-person relationship overlap, influence each other and share the same outcome. Here, positive caregiving and high quality peer or romantic relationships were mostly associated with a higher frequency of Instagram social behaviour (Gobbi et al., 2020; Bonassi et al., 2020b,c, 2021a, 2020a). Within the aforementioned feedback circuit, quality in-person interactions

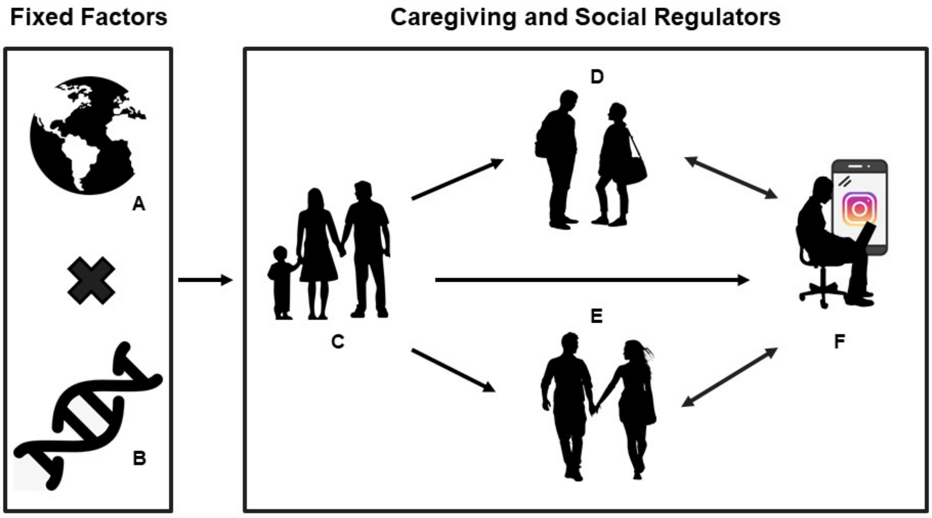

Figure 12: Illustration of the proposed model on the predictors of social behaviour in a developmental perspective. (**A**) Culture and ethnicity as fixed factors present since birth. (**B**) Genome as a set of inherent fixed factors and epigenome as a set of biochemical compounds subject to changes. (**C**), Parent-infant relationship as in-person caregiving factor of adjustment of the trajectory in social development. (**D** and **E**) Peer relationship and romantic relationship as the outcomes and in-person socio-environmental factors of readjustment. (**F**) User-to-user relationship as the outcome and online social factor of readjustment.

This tentative model has combined the results obtained from the studies of the present project to advance a general and coherent data interpretation. Different predictors have been blended into a unique framework to propose a comprehensive architecture of social behaviour. This multifaceted model may merit looking over a combined set of factors (e.g. cultural, genetic, biological, environmental) in affecting in-person and online social experiences. A universal view of sociability could inspire future studies in designing experimental paradigms. However, further research is required to corroborate or confute this potential model. One possibility could be to launch several replication studies starting from the methodologies applied in this project. Another option could be to plan a) novel studies on social media behaviours following a gene-by-culture perspective or b) a comparative analysis between offline and online relationships in an ecological context. Such studies may also highlight alternative interpretations of the theoretical model. Furthermore, it is important to know the limitations of the studies on which the model is based.

5.2 Limitations, Conclusions and Future Directions

The studies belonging to the current research project also presented limitations that are important to consider. An objective analysis of the unsolved issues of the studies allows outlining objective conclusions and designing suitable projects in the future.

First, the sample size was determined by study constraints in the three studies and had a prevalence of the female gender in studies 2 and 3. Although preliminary analysis excluded potential biases, study 1 had an unbalanced number of participants with a higher number of participants in the Singaporean group. The numerosity of the sample represents a challenge in gene-by-environment interaction studies. In the last decade, genetic association studies with limited sample sizes have become the target of increasing concerns related to the small variance explained in variables by one single-nucleotide polymorphisms (e.g., *OXTR* rs53576) (Munafò, 2009; Mitchell, 2018). However, given the difficulty of unravelling the nature of a given psychological construct (e.g., online sociability) in a gene-by-environment perspective, the same experts of the fields cannot provide a definitive and unique solution to this implicit limitation (Munafò, 2009). For instance, the only evidence that oxytocin is a neuropeptide highly involved in a variety of functions (Meyer-Lindenberg et al., 2011) and expressed in several brain regions could exponentially boost the probability of detecting a significant effect (Montag and Reuter, 2014). A large number of loci could explain a given phenotype (Insel, 2010): recent research has established that a large number of human traits is polygenic (Armstrong-Carter et al., 2021). Here, only the genetic candidates *OXTR* rs2254298 and rs53576 were selected with care based on their well-documented functional properties (Chen et al., 2011b), the hypothesis formulated for this study, and the results from previous works in the field (Truzzi et al., 2018; Senese et al., 2019). From a statistical viewpoint, Cohen's rule of interpreting the magnitude of a significant result (Lakens, 2013) gave evidence of effect sizes at different magnitude (small, medium, or large). The effect sizes were also consistent with the post-hoc power estimation. Other studies of behavioural genetics found comparable post-hoc statistical power in a small sample size (Esposito et al., 2017d; Senese et al., 2017). Although it was not possible to maximise the sample size, a conservative approach to data treatment was adopted, and the results were in line with the expected patterns and defined by a reliable statistical magnitude. In an exploratory way, this works deals with gene-environment interactions applied to recent variables from social media (e.g., Instagram social behaviour), thus paving the way for further studies on the common and divergent mechanisms of online and in-person interaction.

Concerning the second limitation, null results for *OXTR* rs53576 or rs2254298 could also occur due to an unbalanced distribution in allele frequency within the sample in the three studies. Limited to the allelic distribution in the total sample of study 1, comprised of both the Italian and the Singaporean sample, the frequency of A/A and G/G homozygotes and A/G heterozygotes was unbalanced, and this may have influenced the outcomes. Given the novelty of the research, study 2 and 3 could define the role played by *OXTR*/rs53576 and *OXTR*/rs224529 on social media behaviour. Further investigation could focus more on the role of *OXTR* as a potential moderator of offline and online social dispositions on SNSs.

A third limitation of the three studies is the cross-sectional approach, which highlighted a weaker reliance on retrospective reporting of parental bonding than a longitudinal one. The self-reported PBI questionnaire provides a retrospective measure of the individual self-perception of attachment, whereas the self-reported ECR-R questionnaire measures the personal expectations of the adult attachment with the partner. Both could lead to influential biases. Alternative paradigms could include: a) observational techniques as a more direct measure of caregiving patterns in an ecological context; b) a longitudinal approach to collect information on parental practices from childhood to adulthood.

Although original (for the Singaporean group) and validated translated (for the Italian group) versions of the questionnaires were utilised, another point for study 1 is that some conceptual understanding issues could have led to different interpretations of the items, hence altering scoring that might have influenced the results.

Finally, for both countries, the sample was composed of undergraduate/postgraduate students, mainly belonging to social science or psychological fields, who happened to be familiar with the theories beneath the study.

Fifth, Instagram data were not adjusted by the participants' time of membership in studies 2 and 3. Although Instagram data were extracted at the same time-point, the studies did not consider the year of the first registration for each Instagram user or the evolution of the online social activity across time (e.g., in terms of short-term daily usage and long-term increased number of posts, followings and followers). While this would have been an interesting variable to include in the analysis, this information is not publicly available and therefore not acquirable with the methods applied here. Obtaining access to this information could correct the number of posts, followers, and followings by the amount of time passed between the date of creation of an account and the instant in which data were extracted. Future works should consider obtaining this information to obtain a more standardised set of variables.

A potential further limitation could be the difficulty of generalising results obtained in studies 2 and 3 to online sociability outside Instagram. The activity of alternative social network sites like Facebook, Twitter, Tik Tok, Reddit Snapchat should be monitored to discover similar or dissimilar patterns of online socialisation.

Furthermore, in studies 2 and 3, participants were not asked to indicate how many followings and followers they know and how often they meet them in daily life. This element could help future studies to link the frequency of social interactions among in-person and online contexts.

Eighth, study 3 did not collect Instagram data from the participants' partners. Being aware of Instagram attitudes on both participant and the partner would allow for comparing the quality in the intimate relationship and the frequency of social media behaviour in terms of posts, followings, followers and SDI. It is worth noting that the same housing conditions of the participants and their availability of technological devices could alter their access to Instagram.

Subsequent research could adopt different variables or indexes to explore the variegated world of Instagram. Overall, future studies should consider advanced interactions between new genetic factors (e.g., genetic polymorphisms of dopamine, vasopressin) and processes (e.g., intergenerational transmission), epigenetics mechanisms (e.g., DNA methylation), environmental factors (e.g., education, socioeconomic status), but also hormonal components (e.g., menstrual stages in women, testosterone levels in men), social characteristics (e.g., group membership) and individual traits (e.g., personality). All together, these variables could grasp common and specific mechanisms that characterise offline versus online social behaviour.

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