The Brain Correlates of Personality and Sex Differences

Brittany Fair
University of Vermont

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THE BRAIN CORRELATES OF PERSONALITY AND SEX DIFFERENCES

A Thesis Presented

by

Brittany Fair

to

The Faculty of the Graduate College

of

The University of Vermont

In Partial Fulfillment of the Requirements
for the Degree of Master of Science
Specializing in Neuroscience

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Thesis Examination Committee:

Robert Althoff, M.D./Ph.D., Advisor
Hugh Garavan, Ph.D., Advisor
Sean Flynn, Ph.D., Chairperson
Margaret Vizzard, Ph.D.
Julie Dumas, Ph.D.
Cynthia J. Forehand, Ph.D., Dean of the Graduate College
ABSTRACT

Personality neuroscience is a rapidly expanding field of study fueled by a growing interest in understanding the structural brain correlates of individual differences in personality. Data on the structural brain correlates of personality are especially lacking from large-scale studies, and are nearly non-existent in the adolescent age group. Furthermore, the role of sex differences in structural brain changes associated with personality are rarely considered. To address this gap in knowledge, this thesis investigates the structural brain correlates of personality and sex differences in structure at age fourteen. A large sample of adolescents (N = 2000) were drawn from the IMAGEN project. Data on adolescents’ puberty status, IQ, and personality were collected through adolescent-reported questionnaires and interviews. The structural brain correlates of personality were examined utilizing personality variables from the NEO Five Factor Inventory (NEO-FFI) and Voxel-Based Morphometry (VBM). Our results showed few correlations between any dimension of the NEO-FFI and regional grey matter volume (GMV). In the total sample, a negative correlation was found for agreeableness and bilateral supplementary motor area (SMA), which was also present in the male subsample. The female sample showed a significant negative correlation between extraversion and the right SMA, and a positive correlation in the left cerebellum. A non-linear effect of extraversion positively correlated with the right precuneus in females. The present study suggests personality traits are not strongly reflected in GMV during adolescence. This thesis includes a discussion on future directions and suggestions for assessing the brain correlates of personality.
ACKNOWLEDGEMENTS

To Hazel. She has so many opinions. Abundant personality in such a small package.

I would like to thank Dr. Hugh Garavan and Dr. Rob Althoff for their expertise, encouragement and support. I would also like to express my gratitude for Dr. Bader Chaarani for his mentorship and Phil Spechler, M.A. for his guidance. Additionally, I would like to thank Dr. Margaret Vizzard, Dr. Sean Flynn and Dr. Julie Dumas for their willingness to serve on my committee. I would also like to thank Dr. Tony Morielli, the director of the Neuroscience Graduate Program, for his continued enthusiasm and support. Lastly, I would like to thank my family members, Tyler Fair, Vickie Grove, David Fair, and Dustin Grossheim, for encouraging me to always follow my dreams.
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Correlations of personality traits and GMV ($p < .05$). a) In the entire sample, GMV in the right superior frontal gyrus, right supplementary motor area (SMA), and left SMA was negatively correlated with Agreeableness (956 voxels). b) In the male sub-sample, GMV in the right SMA, along with the right superior frontal gyrus was negatively correlated with Agreeableness (1,087 voxels). c) In the female sub-sample, GMV in the left middle frontal gyrus, and the left superior frontal gyrus was negatively correlated with Extraversion (1,431 voxels). GMV in the left cerebellum (not pictured) was also positively correlated with Extraversion (625 voxels). d) Non-linear effects were found in the female extraversion group showing a positive correlation in the right precuneus (992 voxels).

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Latent profile analysis (LPA) revealed a) four classes for the male group and b) three classes for the female group. For the male group, class 2 represented 76% of the population, whereas class 2 for the females represented 78% of the population. These groups represent an arguable ‘median’ group for comparison. Class 4 in the male group is not pictured and was dropped from the analysis as the class size was too small to be meaningful ($n = 13$).
CHAPTER 1: LITERATURE REVIEW

1.1. Introduction to Personality Neuroscience

Personality neuroscience is a rapidly progressing field of research. Personality has been used as a key word for more than 138,344 articles in peer-reviewed journals listed in PubMed as of July 21st, 2017. Personality traits are considered relatively stable over time and various situations, thus representing the behavioral tendencies of an individual (Lei, Yang, & Wu, 2015; Nostro, Muller, Reid, & Eickhoff, 2016; Savolainen, Eriksson, Kajantie, Pesonen, & Raikkonen, 2015). Due to the fact that personality traits are highly correlated to psychopathology, there is a growing consensus stressing the importance of understanding the anatomical correlates of personality. Recent advances in neuroimaging such as structural magnetic resonance imaging (MRI) have allowed researchers to begin to uncover the structural brain correlates of personality.

Magnetic resonance imaging is a noninvasive and safe (no radiation) imaging technique used to examine structural and functional brain differences in human populations in vivo. Using principles from nuclear magnetic resonance, MRI detects changes in hydrogen proton signals in water molecules throughout the brain (Mills & Tamnes, 2014). By relying on variations in the signal strength, anatomical MRI provides contrast to distinguish between grey matter (GM), white matter (WM), and cerebrospinal fluid (CSF) in the brain. One approach to investigating the etiology of personality includes examining changes or differences in GM density or volume. Grey
matter primarily contains neuronal dendrites, synapses and cell bodies, and GM is altered throughout the lifespan (Lezak, Howieson, & Loring, 2004) and with the occurrence of psychopathology (Grav, Stordal, Romild, & Hellzen, 2012). Anatomical differences in GM can be quantified by using voxel-based morphometry (VBM) or by surface-based morphometry (SBM). Since the major focus of this study was examining GM volume differences, VBM, which relies on statistical parametric mapping to quantify GM volume, was chosen as the most accessible and appropriate method. Previous studies have examined the relationship between GM and personality traits; however, due to variations in imaging techniques, small sample sizes, ignored sex differences, and few adolescent studies (all of which are discussed below), prior results are conflicting and often contradictory across studies. Therefore, the aim of this thesis is to review the current literature and provide a comprehensive examination of the structural brain correlates of personality in early adolescence using VBM to explore differences in regional GM volume.

1.2. A Brief History of Personality Neuroscience

Theories of personality came to the forefront of psychology research in the 20th century with the popularity of Sigmund Freud and psychoanalysis. Freud hypothesized personality emerged from aggressive and sexual contexts based on a person’s early life (Rettew, 2013). Although Freud’s psychodynamic theories were based on radical concepts, he laid the groundwork for future personality research. In the mid-20th century, psychologist Gordon Allport rejected the idea of psychanalysis and categorized personality into traits (Allport, 1937). Trait theory describes how personality is
distinguished by distinct patterns of behavior, thoughts and emotions. Allport envisioned personality was biologically determined at birth and then altered via environmental factors throughout the lifespan (Rettew, 2013). Allport is known as one of the founding fathers of modern personality psychology (Matthews & Deary, 1998).

The investigation into the neurobiology of personality commenced in 1967 with Hans Eysenck. The Eysenck personality model includes facets of extraversion, neuroticism and psychoticism (Eysenck, 1967). Eysenck believed these traits were biologically related to cortical arousal and autonomic nervous system function (Lu et al., 2014; Maruszewski, Fajkowska, & Eysenck, 2010). Individuals with low extraversion exhibit higher levels of baseline cortisol, while highly neurotic individuals show more stress reactivity via lower thresholds for sympathetic activation (Eysenck, 1967; Rusting & Larsen, 1997). Jeffrey Gray, Eysenck’s collaborator, postulated two major neuronal systems were driving symptoms of anxiety and impulsivity (Gray, 1976). These systems included the Behavioral Inhibition System (BIS) for anxiety and the Behavioral Activation System (BAS) for impulsivity. BIS is associated with the hippocampus, the septal area, and the Papez circuit, whereas BAS is associated with areas of reward and dopaminergic function such as the basal ganglia and the nucleus accumbens (Maruszewski et al., 2010).

Building on the work of Allport and colleagues, Costa and McCrae expanded the definition of personality into five distinct traits and published the NEO Personality Inventory in 1985, which was later revised in 1992. This 240-item questionnaire included
extraversion, neuroticism, openness, agreeableness, and conscientiousness. Extraversion is related to sensitivity to reward and is associated with positive emotions such as enhanced sociability (Blankstein, Chen, Mincic, McGrath, & Davis, 2009; DeYoung et al., 2010). Social tendencies are often related to reward by involving social affiliation or social status (DeYoung et al., 2010). A highly extraverted individual may seek out more social interactions to acquire social reward. The trait neuroticism is characterized by the tendency to experience increased negative emotions, and a heightened sensitivity to impending threat and punishment (DeYoung et al., 2010). Conscientiousness is defined as having a stable pattern of tendencies, including being goal-directed and delaying gratification. Additionally, conscientiousness is considered a candidate epidemiological variable as it can be used to accurately predict longevity, diseases, and health-related behaviors (Bogg & Roberts, 2013). Agreeableness is related to altruism and the ability to understand others’ emotions, while, increased imagination and intellect are distinctive features of high levels of openness (Costa & McCrae, 1992). The definitions for agreeableness and openness are somewhat vague and remain open to interpretation.

1.3. Personality Matters: Physiological and Psychological Correlates of Personality

Personality traits predispose an individual to specific behavioral patterns, which can result in a variety of physiological and psychological outcomes. For example, personality traits are related to psychopathology (Grav et al., 2012; Malouff, Thorsteinsson, & Schutte, 2005; Vittengl, 2017), substance use (Cooper, Agocha, & Sheldon, 2000; Kotov, Gamez, Schmidt, & Watson, 2010), Alzheimer’s Disease (Wilson, Schneider, Arnold, Bienias, & Bennett, 2007) and possibly autism spectrum disorder
(Schwartzman, Wood, & Kapp, 2016). For example, a trend of high neuroticism, low extraversion, low conscientiousness, and low agreeableness are associated with symptoms of mood and anxiety disorders across the literature (Malouff et al., 2005). More specifically, a large-scale ($n = 35,832$) correlative study suggests high levels of neuroticism and low levels of extraversion are associated with depression (Grav et al., 2012). High levels of neuroticism also predict both anxiety and depression nine and eighteen years after the initial personality questionnaire (Vittengl, 2017). Cumulatively, these studies suggest individuals scoring highly in neuroticism are more sensitive to threat and negative emotionality. The combination of high neuroticism and low extraversion are also risk factors for developing eating disorders (Miller, Schmidt, Vaillancourt, McDougall, & Laliberte, 2006). Further, high levels of neuroticism, extraversion, and low levels of conscientiousness are correlated with substance use such as alcohol misuse (Cooper et al., 2000; Kotov et al., 2010). Conversely, high levels of conscientiousness appear to have a protective effect and are associated with an 89% decrease in risk for developing Alzheimer Disease compared to individuals with low levels of conscientiousness (Wilson et al., 2007). Low levels of agreeableness are related to antisocial traits, and possibly conditions such as autism (Schwartzman et al., 2016). Overall, personality traits exhibit strong correlations to mental health, neurodegenerative disease, and possibly neurodevelopmental disorder.

Personality traits are likely related to psychopathology through underlying biological mechanisms that induce the observed variances in behavior (DeYoung et al., 2010; Eysenck, 1967). For example, high levels of neuroticism are associated with less
serotonin 5-HT1A receptor binding than individuals with low levels of neuroticism (J. Hirvonen, Tuominen, Nagren, & Hietala, 2015), while individuals with major depression have less 5-HT1A receptor density (Jussi Hirvonen et al., 2008). Extraversion has been linked with the dopaminergic reward system and is significantly correlated with dopaminergic receptor availability in the bilateral striatum (Baik, Yoon, Kim, & Kim, 2012). The striatum is a crucial component of the reward system in the brain as it participates in expectation and detection of a reward (Martin-Soelch et al., 2001). This suggests individual differences in neuroticism and extraversion may be reflected mechanistically by variations in serotonergic and dopaminergic receptors, respectively.

1.4. Previous Study Shortfalls

There are many inconsistencies across the neuroimaging literature in the field of personality neuroscience. Studies are especially difficult to compare due to differences in methodology including: a diversity of personality scales, discrepancies in imaging techniques, differences in thresholds and methods utilized to correct for multiple comparisons. Additionally, data are lacking from large-scale studies, longitudinal studies, and are nearly nonexistent in the adolescent age group. Lastly, few studies have considered sex differences. Studies for this literature review were chosen based on the key words ‘grey matter’, ‘VBM’, ‘anatomical MRI’, ‘NEO’ and ‘personality’ in order to produce a representative sample of the literature for comparison.
1.4.1 Inconsistencies with Previous Findings

Previous personality literature lacks congruency and many findings conflict. For example, many traits have been associated with the same anatomical regions as other traits (Table 1). Extraversion (Cremers et al., 2011; DeYoung et al., 2010; Omura, Todd Constable, & Canli, 2005; Rauch et al., 2005), neuroticism (Wright et al., 2006), and openness (Hu et al., 2011) have all been associated with structural differences in the orbitofrontal cortex. Both extraversion and neuroticism are associated with anatomical differences in the amygdala (Omura et al., 2005), the striatum (Barros-Loscertales et al., 2006; DeYoung et al., 2010; Forsman, de Manzano, Karabanov, Madison, & Ullen, 2012; Iidaka et al., 2006) and the prefrontal cortex (Blankstein et al., 2009; DeYoung et al., 2010; Forsman et al., 2012; Wright et al., 2006; Yamasue et al., 2008). Further, the direction of the observed correlations is not consistent across studies such that some traits show positive correlations with grey matter, while others show negative relationships (Table 1). For example, while a positive relationship between extraversion and grey matter in the orbitofrontal cortex has been observed across multiple studies (Cremers et al., 2011; DeYoung et al., 2010; Rauch et al., 2005), conflicting literature suggests a negative relationship in this same region (Coutinho, Sampaio, Ferreira, Soares, & Goncalves, 2013). Grey matter and personality trait relationships may also differ depending on sex affiliation (Blankstein et al., 2009). Therefore, it is difficult to localize personality traits to a specific GM brain region or predict the direction of the relationship.
Table 1: Personality trait and anatomical brain region associations

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Positive and Negative Associations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbitofrontal Cortex</td>
<td>† Extraversion (Rauch et al., 2005, DeYoung et al., 2010, Cremers et al., 2011)</td>
</tr>
<tr>
<td></td>
<td>↓ Extraversion (Coutinho et al., 2013)</td>
</tr>
<tr>
<td></td>
<td>↓ Neuroticism (Wright et al., 2006)</td>
</tr>
<tr>
<td>Frontal Cortex (Inferior or Middle Gyri)</td>
<td>↓ Extraversion (Wright et al., 2006, Coutinho et al., 2013)</td>
</tr>
<tr>
<td></td>
<td>† Extraversion whole group and males (Blankstein et al., 2009, Iidaka et al., 2006)</td>
</tr>
<tr>
<td></td>
<td>↓ Extraversion in females (Blankstein et al., 2009)</td>
</tr>
<tr>
<td>Cingulate Cortex</td>
<td>† Extraversion in males (Cremers et al., 2011)</td>
</tr>
<tr>
<td></td>
<td>↓ Extraversion in females (Blankstein et al., 2009)</td>
</tr>
<tr>
<td></td>
<td>↑ Extraversion in males (Cremers et al., 2011)</td>
</tr>
<tr>
<td>Amygdala</td>
<td>† Extraversion (Omura et al., 2005, Cremers et al., 2011)</td>
</tr>
<tr>
<td></td>
<td>↓ Extraversion (Lu et al., 2014)</td>
</tr>
<tr>
<td></td>
<td>↓ Neuroticism (Omura et al., 2005)</td>
</tr>
<tr>
<td></td>
<td>↑ Neuroticism in females (Iadaka et al., 2006)</td>
</tr>
</tbody>
</table>

Inconsistencies across the literature for the personality traits extraversion and neuroticism show both positive and negative associations with grey matter. The upward arrow (↑) indicates a positive correlation between the personality trait and grey matter, while a downward arrow (↓) indicates a negative correlation.
1.4.2 Personality Scales

The term “personality” is widely used to define individual differences in behavior, motivation, emotion, cognition or even a disorder. This lack of consistency stems from the many different scales used in identifying personality. For example, questionnaires such as the NEO Personality Inventory (NEO-PI) (Costa & McCrae, 1992), the Eysenck Personality Questionnaire (Eysenck, 1967), the Temperament and Character Inventory (TCI) (Cloninger, 1994), Zuckerman and Kuhlman Personality Questionnaire (Zuckerman, Kuhlman, Teta, Joireman, & Kraft, 1993), the Multidimensional Personality Questionnaire (Tellegen & Waller, 2008), and the Minnesota Multiphasic Personality Inventory (Camara, Nathan, & Puente, 2000) are all prevalent in current personality research. Although these scales are largely parallel, they lack congruency. For example, while the NEO-PI includes five personality traits, the TCI includes eight and the Eysenck Questionnaire only has 3 measures of personality. Divergent questionnaires could account for the variations in findings across studies, which makes results difficult to compare.

1.4.3 Neuroimaging Techniques

Differences in neuroimaging techniques could account for varying results across previous personality studies. For example, differences in cluster extent thresholds and multiple comparisons testing are often observed across the literature. A cluster is a group of voxels that are connected to neighboring voxels. An uncorrected threshold is the lower limit that clusters are considered significant before correcting for multiple comparisons. When a large quantity of statistical tests are performed, there is a likelihood for false
positives to occur purely by chance. Therefore, correcting for multiple comparisons produces a more stringent corrected threshold that is crucial for accurate results.

Illustrating these concepts, one previous study obtained promising results pertaining to the brain correlates of personality (Table 2); however, these results have rarely been replicated (DeYoung et al., 2010). In this study, an uncorrected threshold of $p < .01$ was used to initially discern clusters (DeYoung et al., 2010). With such liberal thresholding, there is a high likelihood of inflated false-positive rates (Eklund, Nichols, & Knutsson, 2016). Contradicting these results, in a larger study ($n = 277$), personality traits were not associated with any specific regions of grey matter (W. Liu et al., 2013). This study used an uncorrected voxel significance threshold of $p < .001$, which reduces the risk of false positives and is a much stricter threshold than DeYoung et al., 2010, demonstrating the importance of thresholding neuroimaging data.
<table>
<thead>
<tr>
<th>Personality Trait</th>
<th>Brain Region</th>
<th>Region Involved In</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extraversion</td>
<td>Medial orbitofrontal cortex</td>
<td>Processing reward information</td>
</tr>
</tbody>
</table>
| Neuroticism       | Medial temporal lobe, basal ganglia  
Mid-frontal gyrus  
Mid-cingulate gyrus  
Mid-cingulate gyrus, caudate  
Middle temporal gyrus  
Precentral gyrus  
Cerebellum | Threat, punishment, and negative affect           |
| Agreeableness     | Superior temporal sulcus  
Posterior cingulate  
Fusiform gyrus | Process information about the intentions and mental states of other individuals |
| Conscientiousness | Fusiform gyrus  
Middle frontal gyrus | Planning and the voluntary control of behavior         |
| Openness          | none                                              | none                                                   |

*p < .05, corrected for cluster size.

Complex relationships between age, sex, and personality make neuroimaging studies difficult to compare due to differences covariate inclusion and exclusion (Hu et al., 2011). The previously published anatomical studies of personality do not provide a consistent picture of covariate selection strategies. Covariates such as total brain volume, age and sex are typically included, while other covariates such as handedness, puberty status (in adolescent studies) and IQ are less commonly used. Since covariates are possibly predictive of the outcome variable (GM volume in the present study), utilizing relevant covariates could help elucidate clearer anatomical brain correlates of personality.

Differences in subject motion (head movement) can impact the results of neuroimaging data and this motion is one of the most common confounds in
morphometry studies (Power et al., 2012). Due to this variability, there has been increased advocacy for more attention and care when managing this motion (Power et al., 2012). Participant head movement is especially relevant in studies examining pediatric groups, male subjects, and psychiatric populations that tend to fidget while in the MRI machine (Lerch et al., 2017; Pardoe, Kucharsky Hiess, & Kuzniecky, 2016; Power et al., 2012).

Neuroimaging machinery has improved significantly in recent years. Higher resolution is thought to result in the ability to find more localized and reliable results. Thus, comparing studies that utilized a 1.5T vs. 3T scanner may differ simply due to methodological reasons (Scarpazza, Tognin, Frisciata, Sartori, & Mechelli, 2015). Although beyond the scope of this review, differences in segmentation, normalization, and the Gaussian smoothing kernel play a large role in the results of studies (Scarpazza et al., 2015). Standardized protocol is becoming increasingly consequential, especially as the field moves towards large-scale, longitudinal studies with multiple testing sites.

### 1.4.4. Sample Size

Small sample size is an obstacle of many neuroimaging studies of personality. Few moderate or large-scale studies of personality exist in the current literature (Table 3) (DeYoung et al., 2010; J. Liu et al., 2013; Nostro et al., 2016). Sample size can influence both statistical power and prevalence of Type I errors (Fusar-Poli et al., 2014). Larger datasets afford more statistical power, easier classification of outliers, and underlying distributions become unambiguous. A power analysis conducted in G*Power (Faul,
Erdfelder, Buchner, & Lang, 2009) shows, with 80% power (0.8), an effect size of 15% (0.15), and alpha error probability of 0.05 ($p<0.05$) and only 1 predictor, a study would need a sample of at least 55 participants for the multiple regression analysis. Many previous studies do not meet this minimum threshold (Table 3).

**Table 3: Sample sizes across previous personality neuroimaging literature**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size (Subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rauch et al., 2005</td>
<td>14</td>
</tr>
<tr>
<td>Wright et al., 2006</td>
<td>28</td>
</tr>
<tr>
<td>Forsman et al., 2012</td>
<td>34</td>
</tr>
<tr>
<td>Blankstein et al., 2009</td>
<td>35</td>
</tr>
<tr>
<td>Omura et al., 2005</td>
<td>41</td>
</tr>
<tr>
<td>Barros-Loscertales et al., 2006</td>
<td>50</td>
</tr>
<tr>
<td>Coutinho et al., 2013</td>
<td>52</td>
</tr>
<tr>
<td>Iidaka et al., 2006</td>
<td>56</td>
</tr>
<tr>
<td>Hu et al., 2011</td>
<td>62</td>
</tr>
<tr>
<td>Cremers et al., 2011</td>
<td>65</td>
</tr>
<tr>
<td>Lu et al., 2014</td>
<td>71</td>
</tr>
<tr>
<td>DeYoung et al., 2010</td>
<td>116</td>
</tr>
<tr>
<td>Yamasue et al., 2008</td>
<td>183</td>
</tr>
<tr>
<td>Lui et al., 2013</td>
<td>277</td>
</tr>
<tr>
<td>Nostro et al., 2016</td>
<td>364</td>
</tr>
<tr>
<td><em>Fair 2017 Master’s Thesis</em></td>
<td><em>2,000</em></td>
</tr>
</tbody>
</table>

Sample size is important in order to generalize results to a larger population. Small sample sizes and conflicting results make it difficult to form accurate conclusions about the brain correlates of personality. The purpose of this thesis is to provide a comprehensive examination of the brain correlates of personality during adolescence using a large sample of 2,000 subjects. However, a large sample size does not necessarily equate to a better study. For example, if the data is biased in some way, then collecting
more data will not improve results. Thus, it is important to include pertinent covariates to account for variables that potentially influence the dataset. By controlling for age, puberty status, IQ, handedness, and total GM volume, the present study accounts for additional covariance that could potentially impact results.

1.4.5. Sex Differences

Failure to account for sex differences is a common study design limitation in personality neuroimaging research. Sexual dimorphism in regional anatomies of the brain have been reported in numerous studies (Blankstein et al., 2009; Hu et al., 2011). Additionally, sex differences have been consistently seen across studies in regard to the Five Factor personality traits as women tend to score higher on the personality traits than males (Chapman, Duberstein, Sorensen, & Lyness, 2007; Schmitt, Realo, Voracek, & Allik, 2008), with little variance across cultures (Costa, Terracciano, & McCrae, 2001).

Despite these known differences in the sexes, many studies examining personality have used sex as a covariate (DeYoung et al., 2010) or only recruited male subjects (Barros-Loscertales et al., 2006; Forsman et al., 2012; Schweinhardt, Seminowicz, Jaeger, Duncan, & Bushnell, 2009). Recent findings suggest sex differences may play an important role in brain volume differences; however, findings are conflicting and inconsistent across studies. One study found that personality in a female group was positively correlated with regional GMV in the medial frontal gyrus and anterior cingulate cortex, while males showed the opposite effect (Blankstein et al., 2009). However, a larger study of 364 females and males aged 22-36 years old found personality
and GMV correlations only in the male group (Nostro et al., 2016). The authors hypothesized the null finding in the female group could be due to female brains being better characterized by measures of connectivity, instead of grey matter volume (GMV). Due to conflicting findings, the present study examines males and females separately to detect any differences in the structural brain correlates of personality for each sex.

1.4.6. Age Range

The brain undergoes neuronal plasticity throughout the lifespan. Neural substrates are able to adapt and change due to both external and internal events (Maruszewski et al., 2010). Furthermore, the human brain undergoes a reduction in overall size with age (Lezak et al., 2004). Due to this neuronal plasticity and size reduction, personality may change as behavioral tendencies are altered with age (Maruszewski et al., 2010). Although personality traits are considered relatively stable over time (Lei et al., 2015; Nostro et al., 2016; Savolainen et al., 2015), there may be some movement in the level of these traits. Thus, some personality inventories are starting to be considered ‘age specific’ in their design (Maruszewski et al., 2010). A major question remains, however, as to how much these traits evolve throughout the lifespan as the current literature is inconclusive.

Adolescence represents a period of substantial brain development with divergent neural maturation occurring in males and females (Blankstein et al., 2009). Grey matter density peaks in girls around the age of 11, while this peak does not occur in boys until the age of 14 (Jensen & Nutt, 2015). Age affects neuronal growth and development; however, it remains unclear how these changes affect personality. Although early
adolescence is a crucial time of brain development, few neuroimaging personality studies have included the adolescent age group (Table 4).

**Table 4:** Age ranges across previous personality neuroimaging literature

<table>
<thead>
<tr>
<th>Study</th>
<th>Age Range (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rauch et al., 2005</td>
<td>21-34</td>
</tr>
<tr>
<td>Wright et al., 2006</td>
<td>20-34</td>
</tr>
<tr>
<td>Forsman et al., 2012</td>
<td>19-49</td>
</tr>
<tr>
<td>Blankstein et al., 2009</td>
<td>16-17</td>
</tr>
<tr>
<td>Omura et al., 2005</td>
<td>24*</td>
</tr>
<tr>
<td>Barros-Loscertales et al., 2006</td>
<td>18-34</td>
</tr>
<tr>
<td>Coutinho et al., 2013</td>
<td>19-52</td>
</tr>
<tr>
<td>Idaka et al., 2006</td>
<td>22*</td>
</tr>
<tr>
<td>Hu et al., 2011</td>
<td>20-40</td>
</tr>
<tr>
<td>Cremers et al., 2011</td>
<td>21-56</td>
</tr>
<tr>
<td>Lu et al., 2014</td>
<td>19-26</td>
</tr>
<tr>
<td>DeYoung et al., 2010</td>
<td>18-40</td>
</tr>
<tr>
<td>Yamasue et al., 2008</td>
<td>30-40</td>
</tr>
<tr>
<td>Lui et al., 2013</td>
<td>18-62</td>
</tr>
<tr>
<td>Nostro et al., 2016</td>
<td>22-36</td>
</tr>
<tr>
<td><em>Fair 2017 Master’s Thesis</em></td>
<td>13-15</td>
</tr>
</tbody>
</table>

*mean is provided when no age range was specified

In the adolescent age group, prior research suggests high levels of neuroticism and extraversion is positively correlated with regional GMV in the medial frontal gyrus and anterior cingulate cortex in females, while the males show negative associations in these regions (Blankstein et al., 2009). These findings could represent differences in neuronal maturation between the sexes, however, with only 35 participants (Table 3), it is difficult to draw strong conclusions. Although inconclusive, this study suggests females and males may have structural differences during adolescence. Adolescence represents a dynamic period of human development; a time span that we have limited knowledge...
about in regard to personality. With the goal of uncovering the link between brain
development and personality and fill the gap in the literature, this thesis examines GM
volume differences in 2,000 fourteen-year-old males and females.

1.5. Gap and Purpose

Variations in imaging techniques, small sample sizes, ignored sex differences,
and a range of ages have led to inconsistent findings across the field of personality
neuroscience. Based on the state of existing research, this thesis uses an exploratory
approach, rather than hypothesizing specific brain regions, to test for brain correlates
using whole-brain voxel-based morphometry (VBM). The aim of this thesis is to uncover
the structural brain correlates of personality at age fourteen.

In order to provide a thorough investigation of adolescent personality and fill the
gap in the current literature, this thesis takes a variety of novel approaches. First, this
study examines linear and non-linear personality/brain relationships in the entire sample
and then separately for males and females. Secondly, we use extremes in personality to
discern more powerful associations with certain brain regions. An extreme phenotypic
approach has not been used in previous personality studies, as most studies utilize the
traits as discrete continuous variables. However, using extreme phenotypes has been
successful in studying clinical populations, especially in regard to identifying molecular
features of disease (Perez-Gracia et al., 2010). Third, we utilize latent profile analysis
(LPA) to detect personality profiles for each individual subject. Latent profile analysis is
a person-centered statistical method that identifies classes of individuals with similar
scoring patterns (Basten et al., 2013; Merz, 2011). In the field of psychiatry, there is a recent trend to move towards a ‘dimensionality’ approach to better capture individual differences (Montigny et al., 2013). Thus, latent class analyses are becoming more relevant, although remain largely untapped in personality neuroscience. Lastly, we conduct a replication analysis using the large-scale IMAGEN dataset. Overall, this thesis provides a comprehensive examination of the brain correlates of personality in early adolescence using VBM to explore differences in regional GMV.
CHAPTER 2: MAIN BODY

2.1. Introduction

Personality represents the behavioral, emotional, and cognitive tendencies of an individual (Lei et al., 2015; Nostro et al., 2016; Savolainen et al., 2015) and personality neuroscience is a rapidly expanding field of research. Personality traits are strongly associated to psychopathology; thus, it is clinically relevant to understand the anatomical correlates of personality. Utilizing VBM is a common method for examining personality and grey matter (GM) volume relationships. As grey matter contains neuronal dendrites, synapses and cell bodies, it is a neural component of interest in regard to developing psychopathologies. However, variations in imaging techniques, small sample sizes, ignored sex differences, and a range of ages have led to inconsistent findings across the field of personality neuroscience. Due to conflicting prior results, an exploratory approach was utilized to examine regional GM using whole-brain voxel-based morphometry (VBM). The goal of this thesis is to provide a comprehensive examination of the brain correlates of personality during early adolescence.

2.2. Methods

Overview of IMAGEN protocols

Further details of the procedures, ethics, recruitment, standardized instructions for administration of the psychometric and cognitive behavioral measures for the IMAGEN study can be accessed online (https://imagen-europe.com/).
Participants

Data were acquired from 14-year-old adolescents enrolled in the IMAGEN study. Participants were recruited from public and private high schools across 8 European study sites including England (London and Notthingham), Ireland (Dublin), Germany (Berlin, Hamburg, Mannheim and Dresden) and France (Paris). Participants were invited to undergo an MRI scan and complete written and computer-based assessments examining topics such as intelligence, puberty status, and personality. Participants were excluded if they had contraindications for MRI (i.e. metal implants or claustrophobia). After data quality control, data sets of personality and neuroimaging data were available for 2,000 participants. The mean age of the participants was $14.4 \pm 0.4$ years (range: 13-15 years old) with a close gender ratio (N = 1022 females and 978 males, i.e. 51.1% female).

Personality Questionnaire

To assess personality traits, all participants completed the NEO Five Factor Inventory (NEO-FFI) (Costa & McCrae, 1992) at home using the Psytool® platform (Montigny et al., 2013). The NEO-FFI includes 60 questions with 12 items corresponding to each personality trait. The personality traits are neuroticism, extraversion, openness, agreeableness, and conscientiousness.
Psychiatric Symptoms

Psychiatric symptoms were assessed using the validated Development and Well-Being Assessment (DAWBA) interview (Goodman, Ford, Richards, Gatward, & Meltzer, 2000). For each disorder, a band score ranging from 0 to 5 was calculated representing the likelihood of having the disorder (Montigny et al., 2013). A score of 4 or 5 was considered clinically relevant, although no formal diagnoses were made. For eating disorders, the band score represented the likelihood of having a general eating disorder and was not specific to a subtype.

Intelligence Scale

The Wechsler Intelligence Scale was used to measure IQ and was administered by an experimenter at the study center. Verbal IQ was determined by vocabulary and similarities subscales, while performance IQ was established based on block design, matrix reasoning, and digit span subscales. Females showed significantly lower verbal IQ than males (F: 109; M: 112, \( t_{(1998)} = 4.43, p < .001 \)), while there were no significant differences between the sexes for performance IQ.

Puberty Assessment

To account for hormonal and developmental influences, the Puberty Development Scale (PDS) was used to examine the puberty status of the adolescents. Response options were: not yet started (1 point); barely started (2 points); definitely started (3 points); seems complete (4 points); I don’t know (missing) (Carskadon &
Acebo, 1993). The point values were then averaged to create the PDS score. This scale has been shown to have high validity (Carskadon & Acebo, 1993) and reliability (Petersen, Crockett, Richards, & Boxer, 1988).

**MRI Data Acquisition**

Structural MRI was conducted utilizing 3T scanners from a diversity of manufacturers (Siemens, Munich, Germany; Philips, Best, The Netherlands; General Electrics, Chalfont St Giles, UK; Bruker, Ettlingen, Germany) at the eight IMAGEN evaluation sites (Schumann et al., 2010). A 3D T1 weighted magnetization prepared gradient echo sequence based on the University of Southern California’s Alzheimer’s Disease Neuroimaging Initiative (ADNI) protocol ([http://adni.loni.usc.edu/methods/documents/mri-protocols/](http://adni.loni.usc.edu/methods/documents/mri-protocols/)) was used to acquire images. A more detailed description of the specifications, quality control and standardization across sites can be accessed in a previous publication (Schumann et al., 2010). After quality control, GM volumes from 2,000 adolescents were utilized for the analysis of the structural neuroimaging data.

**Data Preprocessing**

Preprocessing of images was performed using Statistical Parametric Mapping 8 (SPM8) (Friston, Ashburner, Kiebel, Nichols, & Penny, 2007). Images were registered to Montreal Neurological Institute (MNI) template space, and segmented into grey matter
(GM), white matter and cerebrospinal fluid tissue groups. The segmented GM data was then scaled by the inverse-Jacobian of the local transformations (i.e., modulated). This allowed for the preservation of a volume measurement. An 8-mm full-width at half maximum Gaussian kernel was used to smooth the spatially normalized and modulated GM data (Montigny et al., 2013). In subsequent statistical analyses, the dependent variable was absolute GMV. Absolute GMV is a measure of volume, not tissue concentration (Ashburner & Friston, 2000).

**Statistical Analysis**

**Personality Multiple Regressions**

Multiple regression analysis was performed in AFNI (Cox, 1996) using voxel-wise GMV as the dependent variable and personality sum scores as the independent variable. Given the collinearity of the NEO-FFI scores, each trait was assessed by a separate GLM. For the analysis on the entire sample (2,000 participants) age, sex, handedness, pubertal development status (PDS), site, IQ, and total grey matter volume (tGMV) were entered as covariates. Age was included to account for brain maturation differences, whereas handedness was included due to functional differences and possible structural differences between people that are left and right-hand dominant (Gao, Wang, Yu, & Chen, 2015). The inclusion of puberty status was considered relevant in order to account for brain maturation and possible hormone differences. Due to the utilization of eight different scanning locations, site was used as covariate in order to account for
differences in scanning machinery. Lastly, IQ was included as it is related to structural brain volume changes (Brouwer et al., 2014), and total grey matter volume of the individual subject was crucial to include as this study examined volume. Sex differences were assessed by running multiple regression analyses separately for females and males. Based on a voxel-wise uncorrected alpha of $p = .001$, a minimum cluster extent threshold was determined to be $k = 518$ contiguous voxels to arrive at a corrected ROI-level alpha of $p = .05$. This thresholding for multiple comparisons is considered relatively ‘strict’ and decreases the prevalence of false positives (Eklund et al., 2016). Therefore, clusters smaller than 518 voxels were not considered significant in this study.

*Personality Non-Linear Effects*

Non-linear relationships were examined using the square of the sum score of each trait as the independent variable. These whole brain voxel-wise regressions were conducted separately for each sex. In these analyses, the non-squared trait was also included to account for linear effects.

*Extreme Phenotypic Approach*

Extreme phenotypes were calculated using the top 10% (98 subjects) and bottom 10% of subjects (98 subjects) scoring on each personality trait. Differences in the extreme phenotypic groups could be driven by mental health conditions due to the numerous correlations in the literature of high and low traits with anxiety, depression, and eating
disorders. Therefore, instances of depression, generalized anxiety, post-traumatic stress disorder (PTSD), autism spectrum disorder, and eating disorder were examined using band scores from the DAWBA. T-tests were then conducted comparing GMVs of the extreme high vs. extreme low groups for each trait. These analyses were conducted separately for males and females.

**Latent Profile Analysis (LPA)**

A latent profile analysis (LPA) was conducted using MPlus version 7.4 (Muthén & Muthén, 1998-2015) in order to examine possible personality trait profiles for each sex. Latent profile analysis is a person-centered method that allows for the identification of classes of individuals with similar scoring patterns or profiles (Basten et al., 2013; Merz, 2011). Optimum personality profiles were determined by examining the Bayesian information criterion (BIC) (measure of model fit), the Bootstrapped Likelihood-Ratio Test (BLRT) (tests for number of classes), and the entropy (measure of classification fit) (Basten et al., 2013). Each individual was assigned to the profile with the highest probability of membership. The individual had to have a probability of at least 75% to be considered for analysis. The profiles were calculated separately for males and females, leaving 731 males and 732 females for subsequent analyses.

**ROI-Level Replication Analysis**

We examined the regions of interest (ROIs) found in another study (n = 364) to explore replication in our large sample of 2,000 adolescents (Table 5) (Nostro et al., 2016). Spherical ROIs were extracted using 3dCalc in AFNI (Cox, 1996) based on the
MNI coordinates provided. Mean values were extracted for each ROI across the male sample as Nostro et al., only found effects in the male group.

**Table 5:** GMV regions correlated with NEO-FFI in males (Nostro et al., 2016)

<table>
<thead>
<tr>
<th>NEO-FFI Trait</th>
<th>Regions</th>
<th>Size in Voxels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroticism</td>
<td>Parieto-occipital sulcus/ Cuneus</td>
<td>6053</td>
</tr>
<tr>
<td></td>
<td>Left fusiform gyrus/ cerebellum</td>
<td>1027</td>
</tr>
<tr>
<td></td>
<td>Right fusiform gyrus</td>
<td>297</td>
</tr>
<tr>
<td>Extraversion</td>
<td>Precuneus/parieto-occipital sulcus</td>
<td>11,001</td>
</tr>
<tr>
<td></td>
<td>Thalamus</td>
<td>621</td>
</tr>
<tr>
<td></td>
<td>Left fusiform gyrus/Cerebellum</td>
<td>213</td>
</tr>
<tr>
<td></td>
<td>Right Cerebellum</td>
<td>444</td>
</tr>
<tr>
<td>Conscientiousness</td>
<td>Left precuneus/parieto-occipital sulcus</td>
<td>491</td>
</tr>
</tbody>
</table>
2.3. Results

Sample Demographics and Personality Scores

The descriptive statistics of sample demographics and personality scores are shown in Table 6. Age was not correlated with any personality measure in the total sample nor when the sample was split by males and females. Females were significantly higher than males on all personality measures (Neuroticism: $t_{(1998)} = -10.63, p < .001$; Extraversion: $t_{(1998)} = -3.72, p < .001$; Openness: $t_{(1998)} = -6.87, p < .001$; Agreeableness: $t_{(1998)} = -6.94, p < .001$; Conscientiousness: $t_{(1998)} = -2.72, p = .007$) as well as puberty status ($t_{(1998)} = -27.68, p < .001$).

<table>
<thead>
<tr>
<th>Measure</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females ($n = 1022$)</td>
</tr>
<tr>
<td>Age ($M \pm SD$) in years</td>
<td>14.4 ± .4</td>
</tr>
<tr>
<td>Handedness (%R)</td>
<td>91%</td>
</tr>
<tr>
<td>Puberty Development Scale</td>
<td>3.2 ± .4</td>
</tr>
<tr>
<td>Performance IQ ($M \pm SD$)</td>
<td>107.4 ± 13.7</td>
</tr>
<tr>
<td>Verbal IQ ($M \pm SD$)</td>
<td>109.1 ± 14.4</td>
</tr>
<tr>
<td>Neuroticism ($M \pm SD$)</td>
<td>24.8 ± 7.4</td>
</tr>
<tr>
<td>Extraversion ($M \pm SD$)</td>
<td>30.4 ± 5.7</td>
</tr>
<tr>
<td>Openness ($M \pm SD$)</td>
<td>27.0 ± 5.8</td>
</tr>
<tr>
<td>Agreeableness ($M \pm SD$)</td>
<td>30.0 ± 5.3</td>
</tr>
<tr>
<td>Conscientiousness ($M \pm SD$)</td>
<td>28.0 ± 6.7</td>
</tr>
</tbody>
</table>
**Personality and Whole-Brain GMV Values in Total Sample**

Across the entire sample, a negative correlation was found between agreeableness and a cluster (956 voxels) in the right superior frontal gyrus/right supplementary motor area (SMA)/left SMA (Figure 1, a) ($r = -0.113, p < .001$), accounting for age, sex, puberty status, handedness, site, IQ, and tGMV.

**Personality and Whole-Brain GMV Analyses Separate for Each Sex**

In the male group, a negative correlation was found between agreeableness and a cluster (1,087 voxels) in the right superior frontal gyrus/right SMA (Figure 1, b) ($r = -0.166, p < .001$), accounting for age, puberty status, handedness, site, IQ, and tGMV. The female group showed a negative correlation between extraversion and the left middle frontal gyrus/left superior frontal gyrus (Figure 1, c) (1,431 voxels) ($r = -0.161, p < .001$) and a positive correlation in the left cerebellum (625 voxels) ($r = 0.141, p < .001$).

**Personality and Non-linear Relationships with GMV Values**

Non-linear effects were found in the female extraversion group showing a positive correlation in the right precuneus (Figure 1, d) (992 voxels) ($r = -0.136, p < .001$), accounting for age, puberty status, handedness, site, IQ, total GMV, and the extraversion sum score. No other non-linear effects were observed in the female or male group.
Figure 1: Correlations of personality traits and GMV ($p < .05$). a) In the entire sample, GMV in the right superior frontal gyrus, right supplementary motor area (SMA), and left SMA was negatively correlated with Agreeableness (956 voxels). b) In the male sub-sample, GMV in the right SMA, along with the right superior frontal gyrus was negatively correlated with Agreeableness (1,087 voxels). c) In the female sub-sample, GMV in the left middle frontal gyrus, and the left superior frontal gyrus was negatively correlated with Extraversion (1,431 voxels). GMV in the left cerebellum (not pictured) was also positively correlated with Extraversion (625 voxels). d) Non-linear effects were found in the female extraversion group showing a positive correlation in the right precuneus (992 voxels).
**Extreme Phenotypes and GMV Values**


Females with high levels of neuroticism showed significantly higher depressive symptoms than females with low levels of neuroticism (Table 7) \((t_{96}) = 3.13, p = .001\). Additionally, females with low levels of extraversion showed significantly higher levels of depressive symptoms \((t_{96}) = 2.28, p = .012\) and generalized anxiety \((t_{96}) = 2.28, p = .012\) than females with high levels of extraversion. Females showed no significant differences in post-traumatic stress disorder (PTSD), autism spectrum disorder, or eating disorder. No significant differences in psychopathology were observed in the male extreme phenotypic groups. No significant association between high and low levels of each personality trait and GMV were observed.
Table 7: DAWBA scores for the extreme phenotypic groups

<table>
<thead>
<tr>
<th>Female Sub-Group</th>
<th>Depression</th>
<th>Generalized Anxiety</th>
<th>Eating Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Levels of Neuroticism</td>
<td>9</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Low Levels of Neuroticism</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>High Levels of Extraversion</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Low Levels of Extraversion</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

Numbers represent the instances of scoring a level of 4 or level 5 on the DAWBA for depression, generalized anxiety, and eating disorder in the female extreme phenotypic personality groups. A score of 4 or 5 was considered clinically relevant for informing this study.

**Latent Profiles and GMV Values**

Latent profile analysis (LPA) revealed four profiles for the male subsample and three profiles for the female subsample (Figure 2). For the male subsample, Class 1 was composed of 8% of the sample \((n = 60)\) and was comprised of individuals with high levels of neuroticism, average levels of openness, and slightly lower levels of extraversion, agreeableness, and conscientiousness. Class 2 composed 76% of the sample \((n = 553)\) and represented individuals with average levels of each personality trait. Class 3 was composed of 14% of the sample \((n = 105)\) and consisted of individuals with slightly lower levels of neuroticism and slightly elevated levels of extraversion, openness, agreeableness, and conscientiousness. Class 4 was composed of 2% of the sample \((n = 13)\) dropped from the analysis as the class size was too small to be meaningful.

For the female subsample, Class 1 composed 13% of the sample \((n = 95)\) and represented individuals with high levels of neuroticism, average levels of openness, and slightly low levels of extraversion, agreeableness, and conscientiousness. Class 2
composed 78% of the sample \((n = 568)\) and represented individuals with average levels of each personality trait. Class 3 was composed of 9% of the sample \((n = 69)\) and consisted of individuals with very low levels of neuroticism and very elevated levels of extraversion, openness, agreeableness, and conscientiousness. Class 1 for the male subsample and class 2 for the female subsample represent arguable ‘median’ groups for comparison. No significant association between personality latent profiles and regional GMV survived cluster threshold correction.
Figure 2: Latent profile analysis (LPA) revealed a) four classes for the male group and b) three classes for the female group. For the male group, class 2 represented 76% of the population, whereas class 2 for the females represented 78% of the population. These groups represent an arguable ‘median’ group for comparison. Class 4 in the male group is not pictured and was dropped from the analysis as the class size was too small to be meaningful ($n = 13$).
ROI-Level Replication Analysis

The only ROI result replicated from Nostro et al., 2016 was the left fusiform gyrus/cerebellum (1,027 voxels). This region was significantly correlated with neuroticism in the male group in our sample ($r = -.071, p = .027$), accounting for puberty status, handedness, site, IQ, and tGMV.
2.4. Discussion

The present study investigated the relationship between personality traits and regional grey matter volume (GMV) in a large sample \((n = 2,000)\) of 14-year-old adolescents. Females had significantly higher scores than males on all personality measures as well as puberty status, which is consistent with the literature (Chapman et al., 2007; Schmitt et al., 2008). Our results showed few significant correlations between any dimension of the NEO-FFI and regional GMV. In the total sample, a negative correlation was found for agreeableness and bilateral supplementary motor areas (SMA). This result was also present in the male subsample suggesting the male subgroup may be driving the whole-group level affects. The SMA is divided into three main anatomical regions: the supplementary eye fields, the supplementary motor area, and the pre-supplementary motor area (Nachev, Kennard, & Husain, 2008). The SMA is not an area we would have hypothesized \(a\ priori\) as its primary role is direct control of bodily movement. However, there is some evidence that the SMA may link cognition to action (‘intent-to-act’) through connections involving the medial limbic cortex and the primary motor cortex (Goldberg, 2010). Therefore, different levels of agreeableness may contribute to the intent to take action. Additionally, not all roles for the SMA are known and this region could contribute to aspects of personality not anticipated.

In the female subsample, there was a negative correlation between extraversion and GMV in the left middle frontal gyrus/left superior frontal gyrus, and a positive correlation in the left cerebellum. The middle and superior frontal gyri are involved in working memory (Vogel et al., 2016), executive function (Ball et al., 2011), along with
social emotion reappraisal (Grecucci, Giorgetta, Bonini, & Sanfey, 2013). A negative relationship between GMV and higher levels of extraversion could be due to more neuronal pruning. These findings also suggest that high levels of extraversion are linked with more cerebellar volume. The cerebellum has been implicated in social cognition across the literature (Van Overwalle, Baetens, Marien, & Vandekerckhove, 2014). Thus, there could exist a relationship between the neuroanatomical features of emotion and social cognition with the trait extraversion.

In the non-linear analysis, the female subsample also showed a positive correlation between extraversion and the right precuneus. Although the exact function of the precuneus is unknown, the location of the precuneus suggests it has diverse connections within the brain (Cavanna & Trimble, 2006). In monkeys, the precuneus is connected to the prefrontal cortex, the SMA, and the cingulate cortex (Cavanna & Trimble, 2006). Previous neuroimaging studies in humans have shown the precuneus is linked with self-awareness (Kjaer, Nowak, & Lou, 2002), episodic memory (Lundstrom et al., 2003), and the ventral aspect is implicated in the default mode network (Zhang & Li, 2012). The precuneus has many presumed functions, and may be related to extraversion, although the mechanism of action remains elusive.

We found few results for linear and non-linear regression analyses in this study. Therefore, an extreme phenotypic approach was used to help elucidate any brain differences between high and low levels of personality traits. Personality is highly correlated with psychopathology, so it is clinically relevant to investigate if certain brain
regions are contributing to personality traits. Notably, utilizing extreme phenotypic groups has been successful in identifying molecular features of disease in clinical populations (Perez-Gracia et al., 2010). Additionally, this analysis is novel as personality is typically only used as a continuous variable. Yet, contrary to expectations, there were no significant results for the extreme phenotypic analyses. Thus, neither the continuous approach nor the extreme phenotypic approach yielded structural correlates of personality in adolescents. Still, it was possible that examination of each individual trait of personality was not adequate to demonstrate structural brain correlates. For this reason, we examined personality using a profile approach that included all of the personality traits.

Latent profile analysis (LPA) is a useful tool for examining the relationship between personality and mental health (Merz, 2011); however, LPAs remain largely untapped in personality neuroimaging research. The use of personality profiles is a holistic approach to personality research as it encompasses the multifaceted dimensionality of human personality. We sought to enhance the current literature by using an LPA approach with measures of brain volume and personality. This study found 3-class (females) and 4-class (males) solutions fit the data; however, we did not find any significant structural brain differences between the latent profiles for either sex. Collectively, the results from the LPA and the extreme phenotypic analyses strongly suggest that personality differences are not underscored by grey matter volume differences, at least in adolescents.
Lastly, we were largely unable to replicate GMV/trait associations from Nostro et al., 2016. The left fusiform gyrus/cerebellum was significantly correlated with extraversion in the male group in the present sample; however, this was the only finding that replicated. A lack of replication could be due to differences in sample demographics, such as age, as well as covariates used for the analysis. Notably, Nostro et al. examined individuals 22-36 years old, while the present study consisted of 14-year-old adolescents. Additionally, Nostro et al. used age, total brain volume, and sex as covariates, whereas, the present study included the addition of puberty status, site, and IQ, which are covariates relevant to our adolescent sample.

Sex differences were important to explore in this study due to conflicting prior literature and to address recent US National Institutes of Health (NIH) concerns stressing the importance of evaluating sex differences. For example, females process pharmacological drugs differently than men (Franconi, Brunelleschi, Steardo, & Cuomo, 2007), females show more reactivity to stress (Handa & McGivern, 2009), and personality research shows females are consistently higher in neuroticism, which is correlated with depression and anxiety (Zinbarg et al., 2016). Sex differences in brain volume may be due to disparities between the sexes in prostaglandins, neurotransmitters, neuronal growth factors, and immune cells that regulate apoptosis, synaptic growth, dendritic branching and neuronal genesis (McCarthey, Pickett, VanRyzin, & Kight, 2015). Due to physiological and psychological differences between males and females, more robust sex differences in this study were expected.
Voxel-based morphometry results are difficult to interpret as volume differences could be due to variation in cortical thickness, surface area, cortical folding, and/or cortical volume (Riccelli, Toschi, Nigro, Terracciano, & Passamonti, 2017). Additionally, a lack of standardized procedures for interpreting GMV differences across previous studies also impacts results. Interpretation of relative volumes remains under current debate. For example, larger-than-average volumes may represent more power to carry out functions in a given region due to increased neuronal populations or dendritic spines. Conversely, smaller-than-average volumes may represent increased efficiency due to neuronal pruning. There is strong evidence an increase in volume is related to better processing. For example, one prominent study examining hippocampal volumes of taxi cab drivers in London found years of navigation experience was strongly correlated with larger GM hippocampal volumes (Maguire, Woollett, & Spiers, 2006). Yet, these results are still correlational. Understanding the molecular and cellular etiology of grey matter changes is a future direction of neuroimaging research.

Overall, this thesis suggests personality in early adolescence is not represented by distinct structural grey matter volumes differences. Although these findings were unexpected, they are congruent with another large-scale \( (n = 277) \) study in the field (W. Liu et al., 2013). Personality may not be localized to specific brain regions as many brain functions are now thought to be distributed and integrated networks (Nostro et al., 2016). A dispersed architecture could decrease local volumetric effects as seen in the present study. This may explain why personality is so strongly correlated with certain
psychopathologies such as anxiety and depression (Grav et al., 2012) while not being represented in specific anatomical regions in the brain.

Due to the lack of anatomical findings in the present study, future studies should consider functional and connectivity differences in personality. For example, personality differences in white matter integrity have been found using the MRI method of diffusion tensor imaging (DTI) (Xu & Potenza, 2012). Diffusion tensor imaging allows researchers to map white matter tractography via water molecule diffusion properties. Individuals with higher levels of neuroticism had significantly less white matter integrity connecting the prefrontal cortex and amygdala, whereas individuals with higher levels of openness had more white matter integrity connecting cortical and subcortical structures such as the dorsolateral prefrontal cortex. These results suggest white matter differences may underlie variations in personality. Individual differences in extraversion were also observed during an emotional attention task using functional MRI (Haas, Omura, Amin, Constable, & Canli, 2006). Higher levels of extraversion were correlated with more neuronal activity in the anterior cingulate cortex, a region implicated in reward anticipation. Resting-state functional connectivity (RSFC) analysis can also provide a glimpse into the brain’s activity during the absence of a task. For example, individuals with high levels of neuroticism showed altered amygdala RSFC in the right occipital face region indicating these individuals may process faces more negatively than others (Kruschwitz et al., 2015). This result may represent differences in stress and resiliency that underlie high and low levels of neuroticism. Future research should continue to explore functional and connectivity differences in personality.
The present study is the first large-scale examination of GM correlates of personality in adolescents. However, several limitations should be considered. First, due to the design of this large study, several scanning locations and brand of scanner were involved, which may impact results. Second, it should be noted that the IMAGEN project includes a homogeneous sample of adolescents as all subjects are Caucasian and from Northern Europe. Thus, results should not necessarily be inferred for all ethnic groups. Additionally, the variable sex was limited by the option of male or female, which may not accurately reflect all personal gender identities.

With the goal of uncovering the link between brain development and personality, this thesis focused on the early adolescent age group. However, the NEO-FFI may not be the most appropriate tool for measuring adolescent personality (Rettew, 2013), for it was originally created for computing adult personality traits (Costa & McCrae, 1992). Additionally, there is evidence the stability of personality traits increases with age. One review of personality throughout the lifespan found personality becomes most stable after 35 years of age (McAdams & Olson, 2010). This suggests specific brain regions relating to temperament and identity may still be developing during adolescence. One notable strength is this study includes that personality measures were rated by the adolescent, not the parent, which tends to be a more accurate account than parent assessment (Aamodt & Wang, 2011). However, if personality fluctuates during early adolescence, then any type of assessment could have challenges and may not perfectly capture an adolescent’s behavioral, emotional, and cognitive tendencies.
There is also a notable difference between the NEO-FFI and the NEO PI-R. While the NEO PI-R contains 240 questions, the NEO-FFI is limited by a shorter 60 item questionnaire (Costa & McCrae, 1992). The NEO PI-R can be used to assess various facets of each trait, while the NEO-FFI is restricted in categorization of solely the five personality factors or domains. Thus, interpretation with the NEO-FFI is limited and may not encompass the dimensionality of an individual’s personality. Although possibly limited in capturing the full extent of personality, the NEO-FFI remains a robustly reliable measure of personality (McCrae, Kurtz, Yamagata, & Terracciano, 2011) and personality remains an important indicator of mental health and substance use (Grav et al., 2012; Matthews & Deary, 1998).

In conclusion, this large-scale study fills the gap in knowledge by examining the brain correlates of personality and sex differences in early adolescence and provides evidence that personality is not represented in specific GM regions, at least in adolescence. Due to such a large sample size ($n = 2000$), this study was not limited by statistical power. The present results help inform hypotheses for future personality research utilizing connectivity and functional methods such as DTI, functional MRI and resting-state. This thesis represents a significant step in the investigation of the anatomical basis of personality.
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