Abstract

Self-regulation is considered a powerful predictor of behavioral and mental health outcomes during adolescence and emerging adulthood. In this dissertation I address some electrophysiological and genetic correlates of this important skill set in a series of four studies. Across all studies event-related potentials (ERPs) were recorded as participants responded to tones presented in attended and unattended channels in an auditory selective attention task. In Study 1, examining these ERPs in relation to parental reports on the Behavior Rating Inventory of Executive Function (BRIEF) revealed that an early frontal positivity (EFP) elicited by to-be-ignored/unattended tones was larger in those with poorer self-regulation. As is traditionally found, N1 amplitudes were more negative for the to-be-attended rather than unattended tones. Additionally, N1 latencies to unattended tones correlated with parent-ratings on the BRIEF, where shorter latencies predicted better self-regulation. In Study 2 I tested a model of the associations between self-regulation scores and allelic variations in monoamine neurotransmitter genes, and their concurrent links to ERP markers of attentional control. Allelic variations in dopamine-related genes predicted both my ERP markers and self-regulatory variables, and played a moderating role in the association between the two. In Study 3 I examined whether training in Integra Mindfulness Martial Arts, an intervention program which trains elements of self-regulation, would lead to improvement in ERP markers of attentional control and parent-report BRIEF scores in a group of adolescents with self-regulatory difficulties. I found that those in the treatment group amplified their processing of attended relative to unattended stimuli over time, and reduced their levels of problematic behaviour whereas those in the waitlist control group showed little to no change on both of these metrics. In Study 4 I examined potential associations between self-regulation and attentional control in a group of emerging adults. Both event-related spectral perturbations (ERSPs) and intertrial coherence (ITC) in the alpha and theta range predicted individual differences in self-regulation. Across the four studies I was able to conclude that real-world self-regulation is indeed associated with the neural markers of attentional control. Targeted interventions focusing on attentional control may improve self-regulation in those experiencing difficulties in this regard.

Keywords: Self-regulation, adolescence, selective attention, event-related potentials, monoamine-related genes
Acknowledgements

I would like to first thank all of the many families and participants who generously donated their time and energy to participate in the four studies described in my dissertation. EEG research is inherently time consuming, and I thank you for all of your patience in completing all computer tasks and questionnaires.

I am also very thankful to my advisor, Dr. Sid Segalowitz, for providing me with the skills and guidance necessary to follow this project through to the end. Without him my passion for cognitive developmental neuroscience would not have flourished to the level that it is today. I appreciate all of his feedback on my writing style and research ability. I would also like to express my sincerest thanks to the members of my thesis committee, Dr. Karen Arnell and Dr. Teena Willoughby for their valuable feedback from beginning to end. Furthermore, I would like to thank my genetics collaborators at the National Institute of Health, Dr. Monique Ernst and her research team, especially Dr. Elena Gorodetsky. Their expertise in genetics was an integral part of this project. To Karen Milligan and the staff at Integra, thank you for letting me get involved in such an exciting project!

I extend my thanks also to the members of BUCANL, both past and present. To James Desjardins, Allison Flynn, and Diane Santesso, without you my dissertation would not have been possible! To Angela Dzyundzyak, Allan Campopiano, Meghan Weissflog, Stefon van Noordt, Julie Baker, and Reno Zheng for their advice, support and friendship these past many years. To Dr.'s Jane Dywan and Tim Murphy, thank you for your wisdom along the way.

Lastly I wish to thank my family and friends for their love and unyielding support throughout my time at Brock University. Thank-you to my father, John Lackner, for instilling my love of psychology in me, and to my many siblings for believing in me. Thanks especially to my husband and fellow psychology lover, Dave Malyk, for his unending support and encouragement. I am very grateful to the rest of the Malyk family: Jen, Bob and Cindy. I thank them for welcoming me into their home and for cheering me on along the way.

This research was funded in part by an Alexander Graham Bell Graduate Scholarship awarded to me by the Natural Sciences Engineering and Research Council of Canada, and a CIHR grant awarded to SJS.
# Table of Contents

1. GENERAL INTRODUCTION .......................................................... 1  
   Physiology of Self-Regulation ...................................................... 3  
   Stages of Attentional Filtering .................................................... 6  
   Monoamine-Related Neurotransmitters ........................................... 8  
      Dopamine (DA) ........................................................................ 8  
      Serotonin (5-HT) ...................................................................... 11  
   Advanced Electrophysiological Data Analysis Techniques .................. 13  
      Inter-trial phase consistency (ITC) and event-related spectral  
      perturbations (ERSP) ............................................................... 13  
      Case study approach ............................................................... 14  
   Theoretical Model ................................................................. 14  
   References ............................................................................. 16  
2. STUDY 1 ........................................................................... 25  
   Methods .................................................................................. 30  
      Participants ........................................................................... 30  
      Materials and Procedures .......................................................... 31  
      Behavior Rating Inventory of Executive Function ..................... 31  
      Selective auditory attention task ................................................ 31  
      EEG recording and data analysis ............................................... 32  
   Results .................................................................................... 33  
      Behavioral Responses and Executive Functioning ...................... 33  
      Electrophysiological Measures .................................................. 34  
      Preliminary Analyses ................................................................. 34  
      EFPs and self-regulatory behaviors - Extreme groups approach .... 35  
      EFPs and self-regulatory behaviors - Exploratory correlations ....... 40  
      N1s and self-regulatory behaviors - Extreme groups approach ....... 41  
      N1s and self-regulatory behaviors - Exploratory correlations ......... 42  
      EFPs, N1s, and self-regulatory behaviors – Dissociable correlates ...... 44  
   Discussion ............................................................................. 45  
   References ............................................................................. 53  
3. STUDY 2 .......................................................................... 60  
   Electrophysiological Correlates of Self-Regulation ......................... 60  
   Genetic Correlates of Self-Regulation ............................................ 61  
      Dopamine (DA) ....................................................................... 61  
      Serotonin (5-HT) ..................................................................... 64  
   Methods .................................................................................. 65  
      Participants ........................................................................... 65  
      Materials ............................................................................... 66  
      Selective auditory attention task ................................................ 66  
      Adolescent Self-Regulation Inventory ......................................... 67  
      Behavior Rating Inventory of Executive Function ...................... 68  
      Self-Administered Rating Scale for Pubertal Development .......... 68  
   Procedure ............................................................................... 69  
      EEG recording and analysis ....................................................... 69  
      Genotyping parameters ............................................................ 69
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMT</strong> haplotype</td>
<td>70</td>
</tr>
<tr>
<td><strong>DRD4</strong> VNTR</td>
<td>70</td>
</tr>
<tr>
<td><strong>DRD4</strong> rs1800955</td>
<td>71</td>
</tr>
<tr>
<td><strong>5-HTTLPR</strong></td>
<td>71</td>
</tr>
<tr>
<td>ERP analysis</td>
<td>73</td>
</tr>
<tr>
<td>Genes and self-regulation</td>
<td>75</td>
</tr>
<tr>
<td>Moderation analysis</td>
<td>75</td>
</tr>
<tr>
<td>Results</td>
<td>76</td>
</tr>
<tr>
<td>Genes and ERPs</td>
<td>76</td>
</tr>
<tr>
<td><strong>DRD4</strong> VNTR</td>
<td>76</td>
</tr>
<tr>
<td><strong>DRD4</strong> rs1800955</td>
<td>78</td>
</tr>
<tr>
<td><strong>COMT</strong> haplotype</td>
<td>80</td>
</tr>
<tr>
<td><strong>5-HTTLPR</strong></td>
<td>82</td>
</tr>
<tr>
<td>Genes and self-regulation</td>
<td>84</td>
</tr>
<tr>
<td><strong>DRD4</strong> VNTR</td>
<td>84</td>
</tr>
<tr>
<td><strong>DRD4</strong> rs1800955</td>
<td>85</td>
</tr>
<tr>
<td><strong>COMT</strong> haplotype</td>
<td>85</td>
</tr>
<tr>
<td><strong>5-HTTLPR</strong></td>
<td>85</td>
</tr>
<tr>
<td>Model test</td>
<td>85</td>
</tr>
<tr>
<td><strong>DRD4</strong> VNTR, the EFP and self-regulation</td>
<td>86</td>
</tr>
<tr>
<td><strong>DRD4</strong> VNTR, the N1 and self-regulation</td>
<td>86</td>
</tr>
<tr>
<td><strong>DRD4</strong> rs1800955, the EFP and self-regulation</td>
<td>86</td>
</tr>
<tr>
<td><strong>DRD4</strong> rs1800955, the N1 and self-regulation</td>
<td>87</td>
</tr>
<tr>
<td><strong>COMT</strong> haplotype, the EFP and self-regulation</td>
<td>87</td>
</tr>
<tr>
<td><strong>COMT</strong> haplotype, the N1 and self-regulation</td>
<td>87</td>
</tr>
<tr>
<td><strong>5-HTTLPR</strong>, the EFP and self-regulation</td>
<td>88</td>
</tr>
<tr>
<td><strong>5-HTTLPR</strong>, the N1 and self-regulation</td>
<td>89</td>
</tr>
<tr>
<td>Follow-up analyses</td>
<td>89</td>
</tr>
<tr>
<td>Discussion</td>
<td>90</td>
</tr>
<tr>
<td>Limitations and future directions</td>
<td>96</td>
</tr>
<tr>
<td>References</td>
<td>98</td>
</tr>
<tr>
<td>4. STUDY 3</td>
<td>107</td>
</tr>
<tr>
<td>Methods</td>
<td>113</td>
</tr>
<tr>
<td>Participants</td>
<td>113</td>
</tr>
<tr>
<td>Measures and Procedures</td>
<td>113</td>
</tr>
<tr>
<td>Integra Mindfulness Martial Arts</td>
<td>114</td>
</tr>
<tr>
<td>Selective auditory attention task</td>
<td>115</td>
</tr>
<tr>
<td>EEG recording and data preprocessing</td>
<td>116</td>
</tr>
<tr>
<td>Behavior Rating Inventory of Executive Function</td>
<td>117</td>
</tr>
<tr>
<td>Data analysis</td>
<td>117</td>
</tr>
<tr>
<td>Electrophysiology</td>
<td>120</td>
</tr>
<tr>
<td>Behaviour</td>
<td>120</td>
</tr>
<tr>
<td>Results</td>
<td>120</td>
</tr>
<tr>
<td>Electrophysiological change over time</td>
<td>121</td>
</tr>
<tr>
<td>Behavioural change over time</td>
<td>130</td>
</tr>
<tr>
<td>Session 1 group comparisons</td>
<td>130</td>
</tr>
</tbody>
</table>
### List of Tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1.1</td>
<td>Results of Multiple Regression Analyses Predicting the BRIEF Subscales and Metacognition Index Subscales from Peak EFP Amplitudes at Fz</td>
<td>41</td>
</tr>
<tr>
<td>Table 1.2</td>
<td>Results of Multiple Regression Analyses Predicting BRIEF Subscales and Behavior Regulation Index Subscales from N1 Latency at CPz</td>
<td>43</td>
</tr>
<tr>
<td>Table 2.1</td>
<td>Allelic Distributions</td>
<td>66</td>
</tr>
<tr>
<td>Table 2.2</td>
<td>Genetic Summary Table</td>
<td>73</td>
</tr>
<tr>
<td>Table 2.3</td>
<td>Genetic Moderation of the Association Between Self-Regulation and the N1 UT Latency</td>
<td>88</td>
</tr>
<tr>
<td>Table 2.4</td>
<td>Genetic Moderation of the Association between Self-Regulation and the EFP UT Amplitudes</td>
<td>89</td>
</tr>
<tr>
<td>Table 3.1</td>
<td>Treatment versus Control Group Scores at session one</td>
<td>130</td>
</tr>
<tr>
<td>Table 3.2</td>
<td>Control Group Change in MI Scores Across Sessions</td>
<td>131</td>
</tr>
<tr>
<td>Table 3.3</td>
<td>Control Group Change in BRI Scores Across Sessions</td>
<td>131</td>
</tr>
<tr>
<td>Table 3.4</td>
<td>Treatment Group Change in MI Scores Across Sessions</td>
<td>132</td>
</tr>
<tr>
<td>Table 3.5</td>
<td>Treatment Group Change in BRI Scores Across Sessions</td>
<td>132</td>
</tr>
<tr>
<td>Table 4.1</td>
<td>Distribution of Cognitive and Emotional Self-Regulation Pre-screening Scores</td>
<td>154</td>
</tr>
<tr>
<td>Table 4.2</td>
<td>Correlations between Pre-screening Measures and BRIEF Measures Collected During the Testing Session</td>
<td>158</td>
</tr>
</tbody>
</table>
### List of Figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1.1</td>
<td>Grand averaged ERP waveforms to attended and unattended stimulus streams</td>
<td>35</td>
</tr>
<tr>
<td>Figure 1.2</td>
<td>Averaged ERP waveforms to attended and unattended stimulus streams for participants in the top and bottom third of the BRIEF distribution</td>
<td>37</td>
</tr>
<tr>
<td>Figure 1.3</td>
<td>Scalp topographies presented as a function of stimulus condition (attended versus unattended) and group (top versus bottom third of the BRIEF)</td>
<td>39</td>
</tr>
<tr>
<td>Figure 2.1</td>
<td><em>DRD4</em> VNTR differences in the EFP at Fz</td>
<td>77</td>
</tr>
<tr>
<td>Figure 2.2</td>
<td><em>DRD4</em> VNTR differences in the N1 at CPz</td>
<td>78</td>
</tr>
<tr>
<td>Figure 2.3</td>
<td><em>DRD4</em> rs1800955 differences in the EFP at Fz</td>
<td>79</td>
</tr>
<tr>
<td>Figure 2.4</td>
<td><em>DRD4</em> rs1800955 differences in the N1 at CPz</td>
<td>80</td>
</tr>
<tr>
<td>Figure 2.5</td>
<td><em>COMT</em> haplotype differences in the EFP at Fz</td>
<td>81</td>
</tr>
<tr>
<td>Figure 2.6</td>
<td><em>COMT</em> haplotype differences in the N1 at CPz</td>
<td>82</td>
</tr>
<tr>
<td>Figure 2.7</td>
<td><em>5-HTTLPR</em> differences in the EFP at Fz</td>
<td>83</td>
</tr>
<tr>
<td>Figure 2.8</td>
<td><em>5-HTTLPR</em> differences in the N1 at CPz</td>
<td>84</td>
</tr>
<tr>
<td>Figure 3.1</td>
<td>Grand averaged waveforms for attended and unattended target tones</td>
<td>123</td>
</tr>
<tr>
<td>Figure 3.2</td>
<td>Results of the single subject bootstrapping procedure for the condition comparison at each testing session for the waitlist control group</td>
<td>127</td>
</tr>
<tr>
<td>Figure 3.3</td>
<td>Results of the single subject bootstrapping procedure for the condition comparison at each testing session for the treatment group</td>
<td>128-129</td>
</tr>
<tr>
<td>Figure 4.1</td>
<td>EFP at Fz collapsed across all participants</td>
<td>159</td>
</tr>
<tr>
<td>Figure 4.2</td>
<td>EFPs as a function of BRIEF tertial and condition</td>
<td>160</td>
</tr>
<tr>
<td>Figure 4.3</td>
<td>N1s elicited to AT and UT stimuli at Cz</td>
<td>161</td>
</tr>
<tr>
<td>Figure 4.4</td>
<td>N1s as a function of BRIEF tertial and condition</td>
<td>161</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>----------</td>
<td>------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Figure 4.5</td>
<td>Intertrial coherence at Fz divided by group and condition</td>
<td>162</td>
</tr>
<tr>
<td>Figure 4.6</td>
<td>ERSPs at Fz, divided by group and condition</td>
<td>163</td>
</tr>
<tr>
<td>Figure 4.7</td>
<td>ITC at Cz divided by group and condition</td>
<td>164</td>
</tr>
<tr>
<td>Figure 4.8</td>
<td>ERSP at Cz divided by group and condition</td>
<td>165</td>
</tr>
</tbody>
</table>
List of Appendices

<table>
<thead>
<tr>
<th>Appendix</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix A</td>
<td>Studies 1 and 2: Participant Package</td>
<td>193</td>
</tr>
<tr>
<td>Appendix B</td>
<td>Selective Auditory Attention Task</td>
<td>200</td>
</tr>
<tr>
<td>Appendix C</td>
<td>Study 2: Genetic Cross-Tabulations</td>
<td>202</td>
</tr>
<tr>
<td>Appendix D</td>
<td>Study 4: Participant Pre-screening</td>
<td>205</td>
</tr>
<tr>
<td>Appendix E</td>
<td>Ethical Clearance</td>
<td>209</td>
</tr>
</tbody>
</table>
List of Abbreviations

5-HT - serotonin
5-HTTLPR - serotonin transporter gene
ACC - anterior cingulate cortex
ADHD - attention deficit/hyperactivity disorder
ANT - attended non-target
APS - average pain sensitivity
ASRI - Adolescent Self-Regulation Inventory
AT - attended targets
BESA - Brain Electrical Source Analysis
BRI - Behavior Regulation Index
BRIEF - Behavior Rating Inventory of Executive Function
CI - confidence interval
COMT - catechol-O-methyltransferase
DA - dopamine
DERS - Difficulties with Emotion Regulation Scale
DNA - deoxyribonucleic acid
DRD4 - dopamine receptor D4
EEG - electroencephalography
EF - executive functions
EFP - early frontal positivity
ERN - error-related negativity
ERP - event-related potential
ERS - Emotion Reactivity Scale
ERSP - event-related spectral perturbations
GEC - Global Executive Composite
HPS - high pain sensitivity
HWE - Hardy-Weinberg equilibrium
ITC - intertrial coherence
LD - learning disability
LPS - low pain sensitivity
MI - Metacognition Index
MMA - Integra Mindfulness Martial Arts
PCR - polymerase chain reaction
Pe - error-related positivity
PFC - prefrontal cortex
PKU - phenylketonuria
SES - socioeconomic status
SLI - Selective Language Impairment
SNP - single-nucleotide polymorphism
UNT - unattended non-target
UT - unattended target
VNTR - variable number tandem repeat
VTA - ventral tegmental area
1. GENERAL INTRODUCTION

As the roaring of the waves precedes the tempest, so the murmur of rising passions announces the tumultuous change.... Keep your hand upon the helm […] or all is lost. (Boyd, 1962; Rousseau, 1762)

The sentiment that adolescence is a time marked by major physiological, emotional, and behavioural change is not new; great philosophers such as Rousseau, above, emphatically articulated their beliefs about this life stage. Perhaps most famously, G. Stanley Hall advanced the position that adolescence is an invariant period of “storm and stress,” characterized by defiance and a lack of self-control (Hall, 1904). In the years since these seminal writings, philosophers and researchers alike have come to understand that this unvarying lack of self-control during adolescence is not universal. Marked increases in the ability to self-regulate occur over this period, yet wide variation across individuals is observed. Some individuals more than others will be characterized by behaviours typical of Hall’s storm and stress view.

Self-regulation, one of the key features Hall thought that adolescents lacked, is defined here as the ability to monitor, evaluate and adjust emotions and behaviours in order to adapt in a healthy way to social, cognitive and emotional challenges. Poor self-regulatory skill during this developmental phase is associated with risk-taking behaviours such as smoking and alcohol induced problem behaviours (Magar, Phillips, & Hosie, 2008), school truancy (Veenestra, 2010), delinquency (Bandura, Caprara, Barbaranelli, Gerbino, & Pastorelli, 2003), and with a range of other outcome variables including anxiety, depression, social incompetence, and poor academic achievement (Buckner, Mezzacappa, & Beardslee, 2009), all outcomes with pronounced individual and societal costs. Previous research has shown that children who have more difficulty inhibiting
emotional impulses and shifting their attention tend to exhibit more externalizing (Rothbart, Ahadi, & Hershey, 1994; Schmidt, Fox, Perez-Edgar, Hu, & Hamer, 2001) and internalizing (Davidson, Jackson, & Kalin, 2000) behaviours.

Before continuing, a point of clarification is required. Executive functions are traditionally defined as the cognitive abilities of working memory and inhibitory control (and sometimes attentional control; Blair & Ursache, 2011), and are typically assessed using lab-based performance measures. This definition overlaps with that of self-regulation, as these executive skills are required for self-regulation in day-to-day contexts (Blair & Ursache, 2011). Underscoring their conceptual overlap, Takeuchi et al., (2013) refer to these skills as Executive Functions during Everyday Events. However, while the terms are sometimes used interchangeably, here I refer to EF as a narrower set of skills and behaviours dependent on the prefrontal cortex (PFC; Morton, 2010). Self-regulation additionally encompasses the application of these skills to real-life contexts allowing healthy adaptation to social, cognitive and emotional challenges. This broader conceptualization of self-regulation is the focus of the present dissertation.

This distinction between lab-based measures of executive function and self-regulation in real-world contexts is an important one. Performance-based measures are frequently inadequate at capturing the severe deficits in executive functioning that are observed in cases of frontal-lobe injury (Eslinger & Damasio, 1985; Goldstein, Bernard, Fenwick, Burgess, & McNeil, 1993; Meyers, Berman, Scheibel, & Hayman, 1992), and their attempts to separate integrated functions into a series of subcomponents does not allow a true representation of the integrated, multidimensional, and non-person-centric behaviour that is demanded in real-world situations (Goldberg & Podell, 2000). Measures used here,
the Behavior Rating Inventory of Executive Function (BRIEF)\(^1\) and Adolescent Self-Regulation Inventory (ASRI), focus on an ecologically valid assessment of adaptive decision making, and are able to assess this important skill set quite readily.

**Physiology of Self-Regulation**

Some support for the notion that the PFC is responsible for modulation or regulation of behaviour has been found. Over the last decade or so, neurophysiological research has linked self-regulation and its associated skills to several regions of the prefrontal cortex (see e.g., Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004, for a review).

Functional magnetic resonance imaging (fMRI) studies of adults reveal substantial involvement of prefrontal regions during performance of executive functioning tasks (Sylvester et al., 2003). The same pattern holds true at earlier stages of development. Children with prefrontal lesions show impairments on lab-based measures of regulatory control and selective attention ability, as well as parent-report measures (e.g., the BRIEF) of self-regulation in daily contexts (Anderson, Jacobs, & Harvey, 2005). Children with clinical conditions such as Tourette’s disorder show concurrent abnormalities in PFC structure and self-regulatory behaviour (Spessot, Plessen, & Peterson, 2004). Thus, the PFC is crucially involved in regulating behaviour.

Given that regions of the PFC associated with regulatory behaviour show structural maturation through the adolescent period (e.g., the dorsolateral prefrontal cortex important for inhibitory control is not mature until around the age of 20; Giedd, 2004), the straightforward hypothesis exists that measures of PFC functioning may be associated with self-regulation through adolescence and emerging adulthood. However, the PFC is a

---

\(^1\) While the BRIEF is titled as a measure of executive function, the nature of the assessment as well as the forematter of the Professional Manual, demonstrate the tool's utility as a measure of self-regulation.
large anatomical area with a variety of functions (Stuss & Levine, 2002), and each of
these areas may show differing developmental trajectories (Rosso, Young, Femia, &
Yurgelun-Todd, 2004) and so it is necessary to specify which of these functions might be
associated with self-regulatory skill.

There are various theories suggesting a plausible linkage between attentional control
functions of the PFC and self-regulation. In one view, controlled attention is simply one
aspect of self-regulation (Fonagy & Target, 2002; Rueda, Posner, & Rothbart, 2004). In
another view, attentional control is seen as a necessary precursor for regulated behaviour
when nondominant cognitions, emotions and behaviours represent a more adaptive
response than those generally maintained by dominant networks, such as those networks
involved with immediate gratification that might not be adaptive over the long term.
Attentional control is thought to engage these more adaptive nondominant networks,
while simultaneously suppressing dominant but inappropriate cognitions, emotions and
behaviours, thus leading to more appropriately regulated responses (MacCoon, Wallace,
& Newman, 2004). In a third view, self-regulation is a necessary precursor for the
development of controlled attention. Ruff and Rothbart (1996) support this position by
noting that young infants are unskilled at regulating either their own behaviour or their
own attention. Across development, children are required to shift from other-regulation to
self-regulation, and Ruff and Rothbart hypothesize that this forces children into
developing skills of attentional control. Irrespective of the specific nature of these
associations, it is clear that attention turned inwards for the direction of thought and
action is a key element of self-regulatory behaviour. Thus, in this PhD dissertation, I
expect that lab-based measures of attentional control will be associated with ecologically
valid measures of self-regulation, specifically during adolescence and emerging adulthood when many changes to these systems are observed, however it is impossible to address which of these three models might be correct without the use of longitudinal data.

Research with clinical populations suggests that event-related potential (ERP) markers of attentional control are associated with self-regulatory behaviour. Attention deficit/hyperactivity disorder (ADHD) is a condition marked by impairments in regulatory skills (e.g., difficulties focusing attention and inhibiting inappropriate behaviours; see Barkley, 1997; Shaw et al., 2007) and recent ERP studies suggest that children with ADHD show abnormalities in their attention related components (e.g., the P3 component elicited in response to task-irrelevant stimuli and the late negativity associated with reorienting attention; Gumenyuk et al., 2005). Additionally, Stevens and colleagues have published a set of papers which examine ERP differences to attended and unattended auditory stimuli in a group of children with selective language impairment who are also known to have deficits in regulatory skills (Im-Bolter, Johnson, & Pascual-Leone, 2006). The neural hallmark of normative selective auditory attention ability is the N100 difference, or N1d, characterized by larger (i.e., more negative) N100s to attended rather than unattended stimuli, at least in adults. Stevens and colleagues report that children with selective language impairment do not show evidence of an N1 difference (Stevens, Sanders, & Neville, 2006). Although these researchers did not directly demonstrate an association between self-regulation and selective attention, their data suggest that clinical populations with impaired self-regulation show concurrent deficits in ERP markers of attentional control. There is some support to suggest that attention-related ERP markers other than the N1 and the P3 may show associations with self-
regulation. The purported N1 difference reported by Stevens and colleagues may actually be indexing something entirely different from the classic N1 effect. Firstly, what they report are differences in a positive going waveform rather than a negativity, and they do not use traditional N1 sites, but rather average across a whole host of sites covering frontal, fronto-temporal, central and temporo-parietal scalp locations. Typically developing children, but not children with SLI showed evidence of attentional modulation of this early frontal positivity (EFP). This suggests that this EFP in addition to traditional N1s may be useful for investigations of attentional control in childhood and perhaps during adolescence. Interestingly, when children in the Stevens et al. study underwent FastForWord (Scientific Learning®) training focusing on oral language skills with concurrent benefits to regulatory skills such as memory, attention, processing speed and sequencing skills, the EFP difference was increased in children with SLI. This suggests that this marker may relate to regulatory skills, and further supports an hypothesized association between self-regulation and ERP markers of attentional control.

Stages of Attentional Filtering

Attentional control can operate on a number of levels, the first being an automatic and reflexive process that can serve to orient an individual towards salient stimuli or filter out irrelevant stimuli, and the second being a more conscious, effortful process that can serve to maintain attention on a salient stimuli, or override the processing of irrelevant information. These processes are sometimes referred to as top-down and bottom-up attentional control. Today we know that both of these perspectives hold some truth. Inhibition of redundant or irrelevant information can occur as early as 50 ms after stimulus presentation, which is according to some scholars, too early for conscious awareness of the stimuli (Freedman et al., 1987; Freedman, Waldo, Bickford-Wimer, &
Nagamoto, 1991), and likely before cortical processing has occurred (Woldorff et al., 1993). Moreover, evidence for attentional modulation can occur after many aspects of featural processing have already occurred (e.g., as late as 300 ms after stimulus presentation; Katayama & Polich, 1999).

Thus, attention and self-regulation may be linked in two ways. Those individuals who are adept at filtering out information very rapidly may also be the same individuals who are able to skillfully regulate their behaviour. On the other hand, attention may only intervene at later stages of information processing, and a prefrontal 'top-down' control of attention may be closely correlated with self-regulation. Adaptive behaviour requires the efficient use of such prefrontally mediated resources (Engel, Fries, & Singer, 2001).

Early and late selection processes do not mature at the same rate\(^2\). Huang-Pollack and colleagues (Huang-Pollock, Carr, & Nigg, 2002) have demonstrated that 9- and 10-year old children engage early selection processes to a greater extent than late selection processes while adults are more proficient at the latter. Therefore, it is important to understand, when in the attentional control process, that attention and self-regulation are linked and how these relationships play out developmentally. In Studies 1 and 3 of this dissertation, I examine the temporal specificity of hypothesized associations between self-regulation and ERP markers of attentional control in a group of healthy adolescents and then a group with disordered self-regulation.

**Physiology of Attention**

Posner's model of attention was originally posited in 1990 and is still a popular model some 20 years later (Petersen & Posner, 2012). This model assumes three major

---

\(^2\) Note that the early and late selection processes that we refer to here are not the same early and late selection models of attention forwarded by Broadbent (1958) and Deutsch and Deutsch (1963).
functions or subdivisions of attention: (1) orienting, (2) detecting, and (3) maintaining or alerting, each with its own anatomical network (Posner & Petersen, 1990). One can orient their attention towards a wide variety of stimulus types, but the most well-understood system concerns orienting one's attention to a visual stimulus. Animal and human studies show that the posterior parietal lobe is particularly important to orienting towards visual objects, by first disengaging attention from its present focus. Animal studies have additionally implicated the lateral pulvinar of the thalamus and the superior colliculus in re-orienting attention to its new target and the early stages of data processing in the new focus of attention (Posner & Driver, 1992; Posner & Petersen, 1990), as well as brain stem structures (Petersen & Posner, 2012). Stimulus detection is thought to be supported by the functions of the anterior cingulate, and this network has recently been renamed to reflect its executive control over attention (Petersen & Posner, 2012; Posner & Driver, 1992; Posner & Petersen, 1990). Maintenance of alert attention seems to be localized to the right hemisphere, and more specifically to right midfrontal regions (Posner & Driver, 1992; Posner & Petersen, 1990). It is the functioning of these last two systems which is of particular interest in the present dissertation.

**Monoamine-Related Neurotransmitters**

In addition to hypothesized associations between electrocortical functioning and self-regulation, there is also reason to believe that neurochemical functioning may be related to self-regulation. Specifically, in Study 2 I include indirect measures of monoamine neurotransmitter functioning as assessed by allelic variation.

**Dopamine (DA).** Dopamine has been extensively studied for its role in psychological processes, and generally shows strong associations with the functions of the frontal lobe.
Physiological explanations for these results rest on the knowledge that most DA innervation originates subcortically from the ventral tegmental area (VTA) and is then projected forward in the brain along several different pathways, including the mesocortical tract which terminates in the dorsal-medial prefrontal cortex (dmPFC), an area both rich in DA receptors and important to regulated behaviour.

Dopamine exerts strong developmental effects. Animal studies have shown DA to influence proliferation and differentiation of precursor cells in regions of embryonic mouse telencephalon, including the PFC (Popolo, McCarthy, & Bhide, 2004), suggesting that this neurotransmitter may have important developmental effects on brain structure and functioning. Indeed, research from Adele Diamond and colleagues supports this assertion. These researchers have conducted many studies on children with phenylketonuria (PKU), a metabolic disorder that decreases available dopamine. These children consistently show impaired performance on tasks that are associated with frontal lobe development (see Diamond, 2001, for a review).

Moreover, a substantial literature connects allelic variants in genes related to dopamine synthesis, degradation and transport to the functioning of the frontal lobes, specifically the DRD4 and COMT genes.

DRD4 is a DA receptor gene that contains a polymorphic number of amino acid sequence repeats (ranging from 2-11) at exon 3. These repeats, called variable number tandem repeats (VNTRs), have implications for a site within the D4 receptor which is hypothesized to influence either the physical binding of DA molecules or signal transduction. Receptors arising from the 7-repeat variant of the gene are less responsive to DA than are receptors arising from the 2- or 4-repeat variants (Asghari et al., 1995).
Also on the *DRD4* gene is a single-nucleotide polymorphism (SNP) with functional consequences for the dopaminergic system. The T variant of the rs1800955 SNP is associated with a reduced initiation of *DRD4* gene transcription (Okuyama et al., 2000).

The *COMT* gene codes for an enzyme which inactivates dopamine by attaching a methyl group to the molecule. This causes a consequent reduction in post-synaptic DA stimulation. There are three specific allelic variants of the *COMT* rs4680 gene created by a base-pair substitution of the amino acid valine for methionine at codon 158 (known as *COMT* rs4680). The Met/Met variant is associated with the least amount of inactivation (and therefore greater levels of synaptic DA) while the Val/Val variant is associated with the greatest amount of inactivation (and therefore the lowest level of synaptic DA (Lachman et al., 1996). However, while rs4680 associations with behaviour are frequently documented in the literature, this base-pair substitution does not fully explain *COMT* activity. A haplotype formed by genotyping A/G rs6269, C/T rs4633, C/G rs4818, and Val/Met rs4680 (all located on the *COMT* gene), explains variation in *COMT* enzymatic activity better than *COMT* rs4680 alone (Nackley et al., 2006). Thus, *COMT* haplotypes are a more comprehensive way of examining the functioning of the *COMT* system. In Study 2 I genotype for *COMT* haplotypes rather than rs4680 variants alone.

Previous research has connected allelic variants in each of these genes to performance on prefrontally mediated executive functioning tasks across development. Executive functioning skills of preschool aged children are correlated with *DRD4* allele length such that a smaller number of repeats, and therefore more responsive dopamine receptors (i.e., more signalling) are associated with better executive functioning performance (Lackner, Sabbagh, Hallinan, Liu, & Holden, 2012). Moreover, several studies have linked allelic
variations in this gene (specifically the 7-repeat allele) to ADHD, which is characterized by deficiencies in executive functioning (see Shaw et al., 2007). A substantial literature connects allelic variations of COMT to performance on the Wisconsin Card Sort Task in adults (Egan et al., 2001; Lipsky et al., 2005) and a directional Stroop task in children (Diamond, Briand, Fossella, & Gehlbach, 2004).

**Serotonin (5-HT).** Like the dopamine system, the serotonin system also projects from subcortical regions forward to areas of the brain associated with executive control. Serotonergic neurons ascend from the rostral and caudal raphe nuclei to the cerebral cortex and limbic system (Jacobs & Azmitia, 1992). Serotonin plays a role in fetal brain development, and more specifically plays a role in key neural developments such as neurogenesis, apoptosis, axon branching and dendritogenesis in the neocortex in particular (Gaspar, Cases, & Maroteaux, 2003; Janusonis, Glunic, & Rakic, 2004; Khozhai & Otellin, 2006). These neural developments continue throughout adolescence but slow down dramatically thereafter (see e.g., He & Crews, 2007).

Serotonergic signaling is largely terminated by reuptake via the serotonin transporter gene (5-HTTLPR). The VNTR section of the 5HTTLPR gene has consequences for the amount of serotonin available for synaptic transmission. The short VNTR allele results in lower expression of the serotonin transporter and the long allele results in higher expression of the transporter. The short allele is associated with greater quantities of available 5-HT and the long allele with smaller quantities of available 5-HT.

Clinical populations where regulatory behaviour is not normative show increased incidence of the long allele (Kent et al., 2002). More specifically, 5-HT related genes have been implicated in the pathophysiology of ADHD and oppositional defiant disorder.
(ODD: Comings et al., 2000), suggesting an association with self-regulation in real-world contexts. The short 5-HTTLPR allele seems to be beneficial for cognitive performance as evidenced by ERPs. For example the short allele has been previously associated with greater error-related negativities (ERNs) in an error-monitoring task, suggestive of stronger performance monitoring (Fallgatter et al., 2004). The N1d effect observed in selective auditory attention tasks may be altogether absent in individuals homozygous for the long/long allele (Bell, Stevens, & Neville, 2010). Genetic variants of serotonin-related genes are also associated with cognitive self-regulation in preschool aged children and in adults (e.g., using lab based measures of executive functioning: Canli et al., 2005; Kochanska, Philibert, & Barry, 2009) as well as electrophysiological responses to errors during an executive functioning task (Fallgatter, Ehlis, et al., 2004). Such specific associations with self-regulation in adolescence have yet to be reported. Thus, allelic variants in 5-HTTLPR may be associated with both neural and behavioural measurements of regulated behaviour.

Overall then, there is evidence to suggest that indices of 5-HT functioning, namely the VNTR of 5-HTTLPR, may be associated with behavioural indices of self-regulation.

There is considerable genetic research focusing on group differences in executive functioning and/or variables related to self-regulation, usually comparing clinical populations to controls. Genetic work within typically developing individuals usually focuses on lab-based tests of executive functioning, and not on real world, naturalistically occurring demonstrations of self-regulation. I wish to address these gaps in the literature especially because during adolescence many changes to these neurotransmitter systems
are occurring, and we know very little about how these genes are associated with behaviour during this developmental phase.

**Advanced Electrophysiological Data Analysis Techniques**

Electroencephalographic (EEG) data contains a wealth of information and up until recently scholars have generally limited themselves to investigations of specific event-related potential components derived from single or small groups of electrode sites. However, technology has advanced such that it is possible to move beyond traditional ERP analyses. Below I outline one advanced electrophysiological technique that I utilize in Study 4 which may shed light on associations between prefrontal functioning and self-regulation in a group of healthy youth.

**Inter-trial phase consistency (ITC) and event-related spectral perturbations (ERSP).** Amplitudes in the averaged ERP can differ across participants because of differences in the amplitude of the electrocortical generators (measured roughly by Event-Related Spectral Perturbations, or ERSP), or because of differences in the consistency of EEG phase angle (ITC). In other words, individuals can differ in the extent to which their neural response is consistent from trial to trial. This electrocortical form of self-regulation may account for behavioural self-regulation on a larger scale, and may relate to monoamine neurotransmitter function. ITC is calculated and plotted as a frequency-by-latency image of the strength of phase locking of EEG signals to particular events of interest (Makeig, Debener, Onton, & Delorme, 2004). In Study 4, I extract measures of ITC and ERSP and associate them with self-regulatory variables of interest.
Case-study Approach

While Studies 1, 2 and 4 use group-based statistics to assess individual differences in self-regulation, in Study 3 I take a robust single-subject approach to ERP data analysis, using bootstrap resampling techniques on all data points. These approaches have been called for by prominent ERP researchers (e.g., Rousselet & Pernet, 2011), and their use allows investigation of idiosyncratic change in treatment effectiveness in the clinical population that is the focus of Study 3. Profiles of clinical change can be highly variable, and this fine-grained analysis approach may illuminate effects that are masked at the group level. Change in a treatment group is contrasted with change in a waitlist control group, and results are interpreted cautiously given our limited sample.

Theoretical Model

In this dissertation, I test a model of the predictors of self-regulation, examining associations between electrocortical markers of attentional control and monoamine related genes in predicting self-regulation. Monoamine related genes may affect self-regulation directly, or indirectly through their influence on EEG/ERP measures of prefrontal cortex function. I examine the following research questions.

a) Do early occurring ERP indices of selective attention predict self-regulation (Studies 1 and 4)?

b) Do monoamine-related genes affect self-regulation directly, or indirectly through their effects on mPFC, cortical connectivity and regional activation as reflected in EEG/ERPs (Study 2)?

c) Do monoamine genes moderate the association between our electrocortical responses and self-regulation (Study 2)?
d) Do ERP measures of selective attention relate to the level of self-regulatory difficulties experienced by adolescents with ADHD and can both early and late ERP measures of selective attention be improved through training (Study 3)?

Overall then, my dissertation focuses on exploring selective attention and its relationship to self-regulation in the real world by taking measures of electrophysiological activation during auditory selective attention tasks and associating them with self- and parent-report measures of self-regulation. Additionally, I examine how monoamine related genes intervene in these associations, and whether these ERP markers are amenable to intervention. The opportunity arose over the course of my PhD to become involved in a side project with a matching age group where the goal of treatment was to explicitly improve self-regulation, and these results have been included here due to their relevance with the current project.

Previous literature has focused largely on group comparisons of clinical and typically developing adolescents, and I take an individual differences approach to examine whether these genetic and electrophysiological associations will be found in a typically developing sample, but also investigate my hypotheses in a clinical population of adolescent boys with ADHD or other documented self-regulation challenges.
References


modulates the brain electrical response for error processing.

Neuropsychopharmacology, 29(8), 1506-1511. doi: 10.1038/sj.npp.1300409


pooled analysis. *Molecular Psychiatry*, 7(8), 908-912. doi:
10.1038/sj.mp.4001100


10.1016/j.paid.2008.03.014


2. STUDY 1

Executive functioning (EF) refers to the ability to monitor and exercise control over one’s inner state during purposeful, goal-directed and problem-solving behavior. These functions have been variously described to include components of working memory, inhibitory control and cognitive flexibility (e.g., Blair & Ursache, 2011). EF skills increase from infancy to adulthood (Casey et al., 1997; Keating & Bobbitt, 1978; Rothbart & Rueda, 2005) and, of particular importance, poor EF during adolescence has been associated with both externalizing (e.g., risk-taking and substance use; Magar et al., 2008) and internalizing behaviors (e.g., anxiety, depression; Castaneda, Tuulio-Henriksson, Marttunen, Suvisaari, & Lonnqvist, 2008) as well as poor academic achievement (Buckner et al., 2009). Multiple neuroimaging and electrophysiological studies suggest that EF is dependent on the prefrontal cortex (e.g., Spessot, Plessen, & Peterson, 2004). Critically, this region is relatively late to mature (see Gogtay et al., 2004; Segalowitz, Santesso, & Jetha, 2010; Steinberg, 2007) which might contribute to the poor self-regulatory skills often observed in adolescents.

There has been considerable speculation that attentional control, the ability to attend to relevant information and suppress the continued processing of to-be-ignored information, is developmentally linked to EF but there are theoretical disagreements with respect to how these linkages might occur. According to Stuss (1992), controlled attention is one aspect of EF which develops alongside other executive functions as

---

3 This study was previously published as Lackner, C., Santesso, D. L., Dywan, J., Wade, T. L., & Segalowitz, S. J. (2013). Electrophysiological markers of selective auditory attention relate to adolescent executive function. Biological Psychology, 93, 325-333. In our original submission of this manuscript we used the term self-regulation, but here it has been changed to executive function. The reviewers insisted on this nomenclature, given the title of our focal measure (The Behavior Rating Inventory of Executive Function). In addition, there have been minor wording changes for purposes of clarification.
prefrontal structures becoming increasingly adult-like across development. In his view, the broad supervisory attentional functions of the frontal lobes direct more specific lower level systems (e.g., those involved in selective and sustained attention) towards a selected goal. Thus, attentional control is a core aspect of EF which shares a common neurodevelopmental trajectory with other components of EF, e.g., the ability to monitor and evaluate behavior. Another view is that of MacCoon, Wallace, and Newman (2004) who consider attentional control to be a necessary precursor of regulated behavior. That is, EF is only possible when appropriately directed attention is used to enhance the activation of non-dominant networks of cognitions, emotions and behaviors when these represent a more adaptive response than the currently active dominant network. A third view is that EF is a necessary precursor of the development of controlled attention. Ruff and Rothbart (1996) support this position by noting that young infants are unskilled at regulating their own behavior and attention but, as children develop, they are required to shift from other-regulation to self-regulation, forcing them to develop attentional control. Despite these different perspectives, most researchers agree that the self-initiated ability to direct attention is key to EF, and this is the focus of the current study.

Selective attention is one aspect of attentional control that involves several stages of information processing, i.e., the differentiation of stimulus streams, the selection of the relevant stimulus stream, the suppression of the irrelevant streams, and the maintenance of attention toward the relevant information (Määttä, Pääkkonen, Saavalainen, & Partanen, 2005). We hypothesize that attentional control, particularly selective attention, is a major predictor of the ability to self-regulate. Clarifying these associations may help us to better understand the cortical processes underlying disorders where both selective
attention and EF are impaired (e.g., attention-deficit hyperactivity disorder; Mayes & Calhoun, 2007; Qian, Shuai, Cao, Chan, & Wang, 2010; Wahlstedt, 2009); psychopathy; Varlamov, Khalifa, Liddle, Duggan, & Howard, 2010).

In the present study, we examined whether selective attention as reflected in event-related potentials (ERPs) during a dual-channel auditory selective attention task relate to EF skill in healthy adolescent’s everyday lives (as assessed by the parent-completed Behavior Rating Inventory of Executive Function™ - BRIEF). Participants were asked to pay attention to one auditory stimulus stream while ignoring the other and were required to identify, by pressing a response button, an infrequent “target” stimulus (i.e., high tone) in the specified attended channel. Recording EEG throughout the task allowed us to use differences in the amplitude and/or latencies of ERPs to stimuli in the attended versus unattended ears as indicators of efficient (or inefficient) attentional control. Engagement with the attended stimuli would be reflected in larger neural ERP responses to attended stimuli while disengagement, or suppression, would be reflected in smaller ERP responses to unattended stimuli.

In such dual-channel auditory selective-attention paradigms, target stimuli elicit the ERP components N1, P2, N2 and P3. Of particular interest, the N1 reflects the activity of the auditory cortex, with later components reflecting further stages of stimulus processing. Nontarget tones normally elicit only the early occurring N1 and P2 (Hillyard, Hink, Schwent, & Picton, 1973; Nager, Estorf, & Munte, 2006; Woods, 1990), suggesting that attentional resources are quickly withdrawn for the non-response-relevant stimuli. In healthy young adults, the N1 component, as observed over midline fronto-central scalp sites, is typically larger for stimuli in the attended stream (Hillyard et al.,
1973; Woods, 1990). Thus, the N1 difference between attended and unattended tones (the N1d effect) is thought to reflect differences in low-level sensory activity (Johnstone, Barry, Anderson, & Coyle, 1996) and this difference in activity is thought to result in the suppression of an attentional response to unattended tones (i.e., an automatic gating mechanism to reduce further processing of irrelevant stimuli; Singhal, Doerfling, & Fowler, 2002).

In young children ages 3 to 8, a similar but non-identical attention effect has been observed. In a series of studies, Stevens and colleagues (Coch, Sanders, & Neville, 2005; Stevens, Fanning, Coch, Sanders, & Neville, 2008; Stevens, Lauinger, & Neville, 2009; Stevens et al., 2006) examined attentional processes in young children. Using a dichotic listening task, different stories were presented to each ear with probes embedded in each story. The children were asked to listen to the story in one ear and ignore the other. In the typically developing children, the probes in the attended stream elicited a larger positive going electrocortical response than those in the unattended stream. This difference occurred between 100 and 200 ms post stimulus onset. The authors speculate that this positive going attention effect is not simply a reversal of polarity of the N1 effect in children, but rather it is the absence of an N1 which sometimes occurs due to the complexity and demands of the task (Coch et al., 2005). One other paper has also reported an attention-sensitive positive going waveform in 5 year olds, and although it is presented graphically, it is not otherwise analyzed or discussed (Bartgis, Lilly, & Thomas, 2003, see Figure 2, panel 1). Stevens and colleagues do not suggest a name for this component, and so here in order to distinguish it from the traditional N1, we refer to it as an early frontal positivity (EFP) based on an examination of its polarity and
topography. Critically, these selective attention effects were reduced in children from lower SES backgrounds, a circumstance often associated with poorer attentional control (Stevens et al., 2009).

Such auditory evoked potentials, at least those elicited by brief click trains, do not become adult-like until age 12 (Ponton, Eggermont, Kwong, & Don, 2000), and the N1 to standard and target tones, although present by age 12, continues to develop until at least the age of 17 (Johnstone et al., 1996). The attention-sensitive EFP has been reported in children as young as 3 and as old as 9 (Bartgis, Lilly, & Thomas, 2003; Coch et al., 2005; Sanders, Stevens, Coch, & Neville, 2006; Stevens et al., 2008; Stevens et al., 2009; Stevens et al., 2006) but is not observed in adults (Coch et al., 2005; Sanders et al., 2006), although the upper age limit on the presence of the EFP is currently unknown. We were interested in whether the EFP would also be evident in our adolescent sample in addition to the more traditional N1 thereby allowing us to better understand maturational effects in these components and the processes they reflect. Given that our participants were 12 to 14 years of age, we expected that we might observe both the EFP and the N1 in response to auditory stimuli.

Most importantly for the present study, we wanted to see whether these indices of early selective attention would relate to parental reports of their adolescent’s ability to engage in self-regulatory behavior (e.g., their ability to control their emotions under stress, to stay on task in the service of achieving some goal). We hypothesized that adolescents showing a pronounced neural differentiation in ERP amplitudes to attended relative to unattended tones along with rapid processing of behaviorally relevant stimuli in the selective auditory attention task would be the same individuals with the highest
levels of EF as evidenced in parent reports on the BRIEF. We chose to employ the BRIEF measure rather than administering lab-based tests of executive function as we were interested in adolescent’s self-regulatory abilities in their day-to-day lives. Previous work has related lab-based measures of EF with lab-based measures of attention control (see e.g., Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001) and with parent-report assessments of regulatory skill (Gerardi-Caulton, 2000; Rothbart, Ellis, Rueda, & Posner, 2003). Our goal was to explore the potential link between attention control as reflected in ERPs with the naturalistic manifestations of EF. Because of the variety of interrelated constructs tapped in any assessment of EF, we wanted to explore which of these might be most strongly related to our neural measures of selective attention, but given the uncertainty of what the EFP versus N1 represents, we did not formulate specific hypotheses beyond this. Moreover, because of the narrow age-range (2 years) used in the present study we did not expect to see evidence of developmental change within our particular sample.

Methods

Participants

Participants consisted of 48 adolescents 12 to 14 years of age (21 female, mean age = 13.1 yrs), after excluding one who had a substantial hearing loss, one with ERP amplitudes more than 2.5 standard deviations above the mean, one with a large number of false positive responses on the behavioral task. One other participant was excluded from analyses involving the Initiate and Working Memory subscales of the BRIEF due to incomplete responses. Participants were recruited based on their prior participation in a cardiovascular health study conducted in the Health Sciences department, Brock University.
Materials and Procedures

Behavior Rating Inventory of Executive Function (BRIEF; Psychological Assessment Resources, Inc). The BRIEF parent report form is an 86-item measure that asks parents to evaluate their child’s daily behavior with respect to eight domains of EF. The overall Global Executive Composite (GEC) is divided into eight theoretically and empirically derived scales which are then combined to form two indices, the Behavior Regulation Index (BRI) and the Metacognition Index (MI). The BRI (subscales: Inhibit, Shift, and Emotional Control) represents the child’s ability to utilize appropriate inhibitory control in the service of shifting cognitive set, modulating emotions, and modulating behavior. The MI (subscales: Initiate, Plan/Organize, Working Memory, Organization of Materials, and Monitor) represents the child’s proficiency at self-managing tasks and self-monitoring. Scores were inverted so that higher scores represented higher levels of regulatory skill.

Selective auditory attention task. Participants were seated in an electrically shielded room. Two digitized sounds were presented using Etymotic ear inserts (Etymotic Research Inc.). These stimuli consisted of a 1000 Hz (88% probability, nontarget) and a 2000 Hz (12% probability, target) 200 ms tones. During an initial practice block, participants were presented with an example of each type of stimulus and asked to perform 10 practice trials whereby sounds were presented with a variable interstimulus interval of 600 to 800 ms randomized across ears. Participants were instructed to attend to one ear only and to ignore all sounds presented to the other ear. While remaining visually fixated on a cross at the centre of the computer screen, they were asked to respond by pressing a number on a key pad when they heard the target tone in the
attended ear, and not to respond otherwise. Task instructions were presented in written form on the computer monitor while concurrently read aloud by a pre-recorded female voice. The test trials included four blocks of 200 trials each. Trial breakdown across the entire task was as follows: forty-eight 2000 Hz tones presented to the attended ear (attended targets), forty-eight 2000 Hz tones presented to the unattended ear (unattended targets), three-hundred and fifty-two 1000 Hz tones presented to the attended ear (attended non-targets), and three-hundred and fifty-two 1000 Hz tones presented to the unattended ear (unattended non-targets). After the completion of each 200-trial block, there was a 20-second break and participants were then asked to switch their ear of attention and to respond to target tones in that ear only. All participants began the task attending to their right ear. The task took approximately 15 minutes to complete and was part of a larger study on adolescent development.

**EEG recording and data analysis.** EEG was recorded at 121 scalp sites (EGI, Eugene, OR) at a sampling rate of 500 Hz with 0.1-100 Hz analog filtering. Impedances were maintained below 50 kΩ throughout recording. Data were re-referenced offline to the average of all sites, filtered offline (1-30 Hz) and corrected for eye movements using the Gratton and Coles procedure (Gratton, Coles, & Donchin, 1983). In addition to manual examinations of the data, trials with artifacts were automatically removed with a ±75 µV criterion, and then averaged into ERP segments of 1000 ms for target tones correctly responded to in the attended and unattended ears separately, including a 200 ms prestimulus baseline. Peak amplitudes and latencies were clearly maximal over midline sites, as is traditionally found for the N1 (Fz, FCz, Cz, CPz, Pz), with focal data analyses conducted at Fz for the EFP and CPz for the N1, sites where each component had its
maximum peak amplitude. The EFP was manually identified and then scored as the most positive peak 65-160 ms following the stimulus. The N1 was scored as the most negative peak 85-215 ms following the stimulus. Additionally, average amplitude values for each site were calculated for each of the 10 ms periods covering the time range of -5 ms to 295 ms, more than spanning the time period during which most auditory components of the ERP occur. These amplitudes were calculated for focal sites of interest. However, examination of the averaged topographical maps indicated the EFP to be widely distributed across the scalp. In order to reduce the likelihood of reporting a finding related to fluctuations at a single channel, we also compared the EFP averaged across 35 frontal and fronto-temporal sites. These 35 contiguous sites were selected to cover all of the major 10-20 sites covering frontal, fronto-temporal and temporal sites located along the medial plane where Coch, Sanders, and Neville (2005) found their attention effects to be the strongest in both children and adults as well as all intermediate sites. Therefore, three sets of variables served as our dependent measures: 1) peak amplitudes and latencies of the EFP and N1, 2) averaged amplitudes of the EFP and N1 for 10 ms bins at midline sites of interest, 3) averaged amplitudes for the EFP and N1 for 10 ms bins collapsed across 35 frontal sites of interest.

**Results**

**Behavioral Responses and Executive Functioning**

Of the 48 target trials in the attended ear, the mean accuracy rate was 37.9 (SD = 9.82) or 79%. Of the 752 trials that did not require a response, mean errors of commission were 24.1 (SD = 32.0) or 3%. False alarms to target tones in the unattended ear (48 trials) occurred on an average of 5.26 trials (SD = 5.19) or 11%. This level of
accuracy is generally in line with what is typically found with adult participants (e.g., Nager et al., 2006). Mean response times on correct trials were 455 ms ($SD = 52.0$).

Pearson correlations were used to examine the relation between behavioral performance on the selective auditory oddball task and self-regulatory skills as reported on the BRIEF. The number of correct responses, number of false alarms, number of errors of omission, and reaction times to targets did not relate to total scores on the BRIEF or to scores on any of the BRIEF subscales, all $r’s < .21$, $p’s > .15$. Additionally, performance measures did not differ as a function of group membership (good versus poor self-regulators), all $p’s > .50$.

Age was not related to scores on any of the BRIEF subscales, in both correlational, all $r’s < .19$, $p’s > .29$, and group-based (comparing those in the top and bottom thirds of the BRIEF distribution), $t(30) = .68$, $p = .50$, analyses.

**Electrophysiological Measures**

**Preliminary analyses.** The waveforms in Figure 1.1 show that across all participants an EFP elicited by target tones is observed and peaks at approximately 100 ms, maximal at Fz (mean peak EFP latency for both AT and UT conditions was 96 ms, $SD = 21$). A paired $t$-test was conducted to determine whether attended and unattended EFP peak amplitudes, collapsed across all participants, differed from one another. It revealed that, at 100 ms (the time of the EFP amplitude peak) there was no difference in amplitude between the EFPs elicited by attended ($M = 1.50$, $SD = 1.98$) versus unattended ($M = 1.48$, $SD = 1.84$) stimuli, $t(46) = .76$, $p = .45$.

A centrally located N1 component was also identified, beginning at approximately 120 ms and continuing until approximately 180 ms, maximal at CPz
(mean peak N1 latency for both AT and UT conditions was 141 ms, $SD = 23.5$) (see Figure 1.1). A paired $t$-test, collapsed across all participants, indicated that N1 amplitudes to attended channels ($M = -5.17$, $SD = 3.25$) were greater than N1 amplitudes to unattended channels ($M = -3.63$, $SD = 2.06$), $t(47) = 3.01$, $p = .004$, $\eta^2 = .16$, as is traditionally found (Hillyard et al., 1973; Nager et al., 2006).

*Figure 1.1.* Grand averaged ERP waveforms to attended and unattended stimulus streams. The early frontal positivity (EFP) was maximal at Fz for all participants, while the N1 was maximal for all participants at CPz.

**EFPs and self-regulatory behaviors - Extreme groups approach.** In order to characterize differences in EFP activation as a function of EF, we employed two strategies – an extreme groups approach and an exploratory correlative approach including all participants (discussed later). In this extreme groups approach, we first rank-
ordered participants according to their scores on the BRIEF GEC and then divided them into thirds with higher scores indicating better EF. Grouping participants based on their relative position in some individual difference distribution is common in ERP studies associating individual differences with brain activation (see e.g., Jetha, Zheng, Schmidt, & Segalowitz, 2012; Luu, Collins, & Tucker, 2000). A visual inspection of Figure 1.2 shows ERP differences as a function of regulatory skill and condition. Individuals in the top third of the BRIEF distribution (good self-regulators, \( n = 18 \)) showed an EFP to attended stimuli continuing until 120 ms. The magnitude of this peak-scored activation (\( M = 1.43 \pm .48 \mu \nu \)) is slightly diminished in individuals in the bottom third of the distribution (poor self-regulators, \( n = 16; M = 1.22 \pm .42 \)). EFPs are also observed to unattended stimuli. Individuals in the bottom third of the BRIEF distribution (\( M = 2.34 \pm .51 \mu \nu \)) produced a stronger unattended EFP response than those in the top third of the distribution (\( M = .81 \pm .41 \mu \nu \)). Those in the middle third of the distribution are not depicted in Figure 1.2 as their neural responses were highly variable and thus a group average would not be a good characterization of their responding.
In order to further examine these relationships, we compared those scoring in the highest and lowest third of the GEC distribution, with a mixed model ANOVA on peak EFP amplitudes with Condition (attended, unattended) as the within-subjects factor and Group (high third, low third) as the between-subjects factor. As stated previously, there was no main effect for Condition, $p = .54$. However, a significant Condition x Group interaction emerged, $F(1, 30) = 4.62, p = .04, \eta^2 = .13$. Whereas peak EFP amplitudes to attended stimuli did not vary across groups, $t(31) = .33, p = .75$, EFP amplitudes to unattended stimuli were highest for the poor regulators, $t(31) = 2.41, p = .022, d = .79$ (Figure 1.2). Despite what appear to be very early differences between groups, these early apparent differences are not reliable: Examining the average voltage over each 10 ms period starting from 5 ms before the stimulus onset, the observed EFP showed no significant group x condition interactions until the 95-105 ms epoch, and these interactions then continued until 125 ms. Only those in the top-third group showed a
significant attention effect in this time window (all $p$’s < .04). EFP latencies were not associated with GEC scores or subscale scores, all $p$’s > .19, and therefore are not discussed further.

As depicted in Figure 1.3, it appears that there are group topographical differences to stimuli in the unattended channel such that good self-regulators show a diminished EFP in comparison to poor self-regulators who seem less able to inhibit the processing of this to-be-unattended information. Therefore, in addition to looking for group and condition differences in maximal ERP amplitude, we also looked for group and condition differences in frontal activation patterns within specific time frames. Average amplitude values for each of the 10 ms periods covering the time range of our observed EFP as well as the onset of the attention effect observed in Coch, Sanders and Neville (2005) (65-75 ms, 75-85 ms, 85-95 ms, 95-105 ms, 105-115 ms, and 115-125 ms) were the focus of the following ANOVA. For each 10 ms time range, the amplitudes were averaged across 35 frontal sites (see Methods section for selection criteria) producing a single score for each time period (see Figure 1.3 for a depiction of those sites). A 6 (time) x 2 (condition) x 2 (group) mixed-model ANOVA revealed a significant 3-way interaction, $F(5,160) = 3.38$, $p = .006$, $\eta^2 = .10$.

In order to quantify this interaction, we calculated attended-minus-unattended difference scores for each of the six time windows and ran a 6 (time) x 2 (group) mixed-model ANOVA on these values. A significant time x group interaction emerged, $F(5, 28) = 2.55$, $p = .05$, $\eta^2 = .28$. Bonferroni-corrected pairwise comparisons showed that at each of the time windows between 95 and 125 ms, those in the top third of the BRIEF distribution showed a greater distinction between attended and unattended streams than
those in the bottom third of the distribution, all $p$’s < .05. Thus, while good self-regulators are able to “shut-off” the EFP to unattended stimuli by 95 ms, poor self-regulators are unable to inhibit the processing of the unattended stimuli and this shows up during this early time period.

Figure 1.3. Scalp topographies presented as a function of stimulus condition (attended versus unattended) and group (top versus bottom third of the BRIEF). Topographies shown here cover the time period of the observed early frontal positivity (EFP). The statistical comparison of signal averaged over the frontal sites involved the 35 sites highlighted in the topography at the bottom.
**EFPs and self-regulatory behaviors - Exploratory correlations.** We ran a series of simultaneous multiple regression analyses using the entire group to explore the ability of the EFP component at Fz in the attended and unattended conditions to predict unique variability in BRIEF scores. This involved entering the peak-scored EFPs associated with both attended and unattended information into the regression analysis simultaneously to predict each BRIEF scale, and then examining the independent contribution of each condition (attended vs. unattended) to the prediction of parental ratings of their adolescent child on each of the BRIEF scales by examining the \( t \)-test associated with each variable’s beta weight. We chose to enter peak-scored amplitudes into the regressions rather than averaged amplitude values in order to simplify the number of possible regressions presented here. However, averaging together amplitudes at Fz across the entire period where the EFP attention effect occurred (95 to 125 ms) and entering these values into regressions predicting BRIEF scales yielded the same pattern of results as those of the peaks.

As stated earlier, the overall BRIEF composite, the GEC, can be divided into two indices, the MI (metacognition index, i.e., planning/organization) and the BRI (behavioral regulation index, i.e., inhibitory control), and we asked whether these specific scales would be the source of the correlation. Peak EFP amplitudes were not associated with the MI, \( F(2, 44) = 1.71, p = .19 \), the BRI, \( F(2, 44) = .42, p = .66 \), or the composite GEC, \( F(2, 44) = 1.27, p = .29 \) in the overall model. However, as indicated in Table 1.1, there was a trend associating EFP amplitudes to unattended stimuli with unique variance in MI scores, \( t(44) = 1.83, p = .07 \), such that larger unattended EFPs were associated with poorer EF. Table 1.1 presents the results of regression analyses on all subscales making
up the MI. As indicated in the table, EFP amplitudes to unattended stimuli (adjusted for amplitudes to attended stimuli) accounted for unique variance in the following MI subscales: Initiate, Plan/Organize, and Working Memory. In all cases, larger EFP amplitudes to unattended stimuli were associated with poorer self-regulatory skill. EFP amplitudes to attended stimuli did not account for unique variance in the BRIEF subscales. These results were unchanged when age was also entered into the regression analyses.

Table 1.1: Results of Multiple Regression Analyses Predicting the BRIEF Subscales and Metacognition Index Subscales from peak EFP Amplitudes at Fz

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Condition</th>
<th>β</th>
<th>t</th>
<th>Sig.</th>
<th>Zero-order correlation</th>
<th>Partial correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEC composite</td>
<td>AT</td>
<td>.13</td>
<td>.83</td>
<td>.41</td>
<td>.07</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td>UT</td>
<td>-.23</td>
<td>-1.52</td>
<td>.13</td>
<td>-.20</td>
<td>-.22</td>
</tr>
<tr>
<td>BRI composite</td>
<td>AT</td>
<td>.12</td>
<td>.78</td>
<td>.44</td>
<td>.10</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td>UT</td>
<td>-.10</td>
<td>-.66</td>
<td>.51</td>
<td>-.07</td>
<td>-.10</td>
</tr>
<tr>
<td>MI composite</td>
<td>AT</td>
<td>.11</td>
<td>.75</td>
<td>.46</td>
<td>.04</td>
<td>.11</td>
</tr>
<tr>
<td></td>
<td>UT†</td>
<td>-.27</td>
<td>-1.82</td>
<td>.07</td>
<td>-.24</td>
<td>-.27</td>
</tr>
<tr>
<td>MI subscales:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiate</td>
<td>AT</td>
<td>.05</td>
<td>.35</td>
<td>.73</td>
<td>-.02</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>UT*</td>
<td>-.30</td>
<td>2.0</td>
<td>.05</td>
<td>-.29</td>
<td>-.29</td>
</tr>
<tr>
<td>Plan/organize</td>
<td>AT</td>
<td>.14</td>
<td>.99</td>
<td>.33</td>
<td>.06</td>
<td>.15</td>
</tr>
<tr>
<td></td>
<td>UT*</td>
<td>-.31</td>
<td>-2.12</td>
<td>.04</td>
<td>-.27</td>
<td>-.30</td>
</tr>
<tr>
<td>Working Memory</td>
<td>AT</td>
<td>.09</td>
<td>.63</td>
<td>.53</td>
<td>.01</td>
<td>.09</td>
</tr>
<tr>
<td></td>
<td>UT*</td>
<td>-.31</td>
<td>-2.10</td>
<td>.04</td>
<td>-.29</td>
<td>-.30</td>
</tr>
<tr>
<td>Organization of Materials</td>
<td>AT</td>
<td>.16</td>
<td>1.09</td>
<td>.28</td>
<td>.12</td>
<td>.16</td>
</tr>
<tr>
<td></td>
<td>UT</td>
<td>-.19</td>
<td>-1.26</td>
<td>.21</td>
<td>-.15</td>
<td>-.18</td>
</tr>
<tr>
<td>Monitor</td>
<td>AT</td>
<td>-.04</td>
<td>-.27</td>
<td>.79</td>
<td>-.06</td>
<td>-.04</td>
</tr>
<tr>
<td></td>
<td>UT</td>
<td>-.06</td>
<td>-.38</td>
<td>.71</td>
<td>-.07</td>
<td>-.06</td>
</tr>
</tbody>
</table>

Abbreviations: β – standardized beta values. AT – attended, UT – unattended.
† Near significant association, p <= .07.
* p ≤ .05.

N1s and self-regulatory behaviors – Extreme groups approach. We employed a similar analysis strategy to that described above in order to look at associations with the
N1. In the extreme groups ANOVA analysis, attended and unattended peak-scored N1 amplitudes (as measured at CPz) did not differ for top and bottom BRIEF positions, \( ps > .16 \). These null results were repeated using averaged amplitudes at CPz from 125 to 165 ms (the peak timing and location of the N1), \( ps > .7 \).

Despite these null results during the timing of the N1, Figure 1.2 seems to show some evidence of an attention-related effect both just prior to the N1 at Cz and after the peak of the N1 at both Cz and CPz, especially in the bottom third group. Averaged amplitudes for 10 ms bins at these sites were used for exploratory analyses of attention and group effects with these timings. Three separate 3-way ANOVAs were used to explore these potential effects. Beginning at 5 ms before stimulus onset and extending until 105 ms (where the N1 begins to become dramatically more negative) there was no significant 10 (time) x 2 (group) x 2 (condition) interaction at Cz, \( p > .65 \). To explore post-N1 attention effects we looked at the averaged amplitudes for Cz and CPz during 10 ms bins beginning just before the peak of the N1 (125 ms) and extending to 245 ms where in Figure 1.2 the attention effects appear to have dissipated. At both Cz and CPz a three-way 12 (time) x 2 (group) x 2 (condition) interaction was not observed, \( ps > .19 \) and \( .44 \) respectively. However, at Cz a significant group x condition interaction was observed for all time bins beginning at 175 and extending until 245 ms, \( ps < .05 \). At CPz, significant group x condition interactions were observed at 195 -205 ms and 215 – 225 ms, all \( ps < .05 \). During these post-N1 time windows, only the bottom third group showed a significant attention effect.

**N1s and self-regulatory behaviors – Exploratory correlations.** In the regression analyses, peak scored N1 amplitudes did not show any associations with
BRIEF GEC scores (or its subscales), all $p$’s > .10. Averaged N1 amplitudes at CPz from 125 to 165 ms (the peak timing of the N1) also did not show any associations with BRIEF GEC scores (or its subscales). Nonetheless, as can be seen in Table 1.2, regression analyses revealed that shorter N1 latencies to unattended stimuli (adjusted for latencies to attended stimuli) approached significance in predicting the GEC, driven by a significant relation with the BRI, $t(45) = 2.26$ $p = .03$, suggesting that speeded N1 responses to unattended stimuli are associated with the inhibitory aspects of EF, especially the Inhibit and Emotional Control subscales. This pattern of results remained the same when age was entered as a covariate in the regression analyses.

Table 1.2: Results of Multiple Regression Analyses Predicting BRIEF Subscales and Behavior Regulation Index Subscales from N1 Latency at CPz

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Condition</th>
<th>$\beta$</th>
<th>$t$</th>
<th>Sig.</th>
<th>Zero-order correlation</th>
<th>Partial correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEC composite</td>
<td>AT</td>
<td>-.12</td>
<td>-.84</td>
<td>.40</td>
<td>-.16</td>
<td>-.12</td>
</tr>
<tr>
<td></td>
<td>UT†</td>
<td>-.26</td>
<td>-1.84</td>
<td>.07</td>
<td>-.28</td>
<td>-.26</td>
</tr>
<tr>
<td>MI composite</td>
<td>AT</td>
<td>-.19</td>
<td>-1.30</td>
<td>.20</td>
<td>-.22</td>
<td>-.19</td>
</tr>
<tr>
<td></td>
<td>UT</td>
<td>-.20</td>
<td>-1.40</td>
<td>.17</td>
<td>-.23</td>
<td>-.20</td>
</tr>
<tr>
<td>BRI composite</td>
<td>AT</td>
<td>.03</td>
<td>.21</td>
<td>.84</td>
<td>-.02</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td>UT*</td>
<td>-.33</td>
<td>-2.26</td>
<td>.03</td>
<td>-.32</td>
<td>-.32</td>
</tr>
<tr>
<td>BRI subscales:</td>
<td>Inhibit</td>
<td>AT</td>
<td>.04</td>
<td>.29</td>
<td>.78</td>
<td>-.01</td>
</tr>
<tr>
<td></td>
<td>UT*</td>
<td>-.37</td>
<td>-2.61</td>
<td>.01</td>
<td>-.36</td>
<td>-.36</td>
</tr>
<tr>
<td></td>
<td>Shift</td>
<td>AT</td>
<td>-.14</td>
<td>-.99</td>
<td>.33</td>
<td>-.17</td>
</tr>
<tr>
<td></td>
<td>UT</td>
<td>-.20</td>
<td>-1.38</td>
<td>.18</td>
<td>-.22</td>
<td>-.20</td>
</tr>
<tr>
<td></td>
<td>Emotional Control</td>
<td>AT</td>
<td>.12</td>
<td>.84</td>
<td>.40</td>
<td>.08</td>
</tr>
<tr>
<td></td>
<td>UT†</td>
<td>-.26</td>
<td>-1.79</td>
<td>.08</td>
<td>-.24</td>
<td>-.26</td>
</tr>
</tbody>
</table>

Abbreviations. $\beta$ – standardized beta values. AT – attended, UT – unattended.
† Near significant association, $p \lesssim .09$.
* $p \leq .05$.
EFPs, N1s, and self-regulatory behaviors – Dissociable correlates. The exploratory correlative analyses described above appeared to show that the MI and BRI have somewhat dissociable neural correlates, namely EFP amplitudes and N1 latencies respectively. In order to determine whether including the N1 latencies, for example, modified the EFP’s prediction of the MI, we computed two final series of regression analyses where for one set the N1 latencies were entered into a first block predicting the MI scales, followed by the EFP amplitudes in the second block; and a second set of regressions where the EFP amplitudes were entered into a first block predicting the BRI scales, followed by the N1 latencies in the second block. The two electrophysiological measures are not zero-order correlated with one another, \( r(48) = -.04, p = .79 \), and thus we would not expect that controlling for them in the regression analyses above would change our results dramatically.

We first examined whether including these additional ERP measurements in the regressions changed the predictive value of the model. When predicting MI subscales, adding N1 latencies into the regression analyses decreased the predictive value of the EFP only slightly (between .4 and 1.9% less variance accounted for depending on the scale). In the original model the EFP predicted approximately 9% of the variance in each of the initiate, working memory and plan/organize subscales of the MI. Including the N1 latencies reduced this value to 7.8% of the variance accounted for. The strength of the specific associations between UT EFP amplitudes and the MI subscales was virtually unchanged, with \( p \) values in the original model ranging from .04 to .05 and \( p \) values in this modified model ranging from .05 to .07. When predicting BRI subscales, adding EFP amplitudes into the regression analyses increased the predictive value of the N1 latencies.
only slightly (between .6 and 1.5% more variance accounted for depending on the scale). In the original model N1 latencies accounted for an average of 9.8% of the variance in BRI subscales. Including EFP amplitudes in the model allowed 10.9% of the variance to be accounted for. N1 UT latencies were associated with BRI subscales in the original models at the $p$ equals .02 to .07 level. Including EFP amplitudes into the model changed little, with the N1 UT amplitudes predicting BRI subscales at the .01 to .07 level. Because both the EFP and the N1 did not contribute significant independent variance to their respective predictions, we can say that they appear to show somewhat different psychological correlates.

**Source generator modeling.** The high density montage of our ERPs permit attempts at source generator modeling. Given the topographical pattern of the EFP, one would expect sources to be frontal. In order to derive such models, we employed BESA (version 5.1.8) with a 4-shell ellipsoidal model over the period of 60 to 100 ms for the two group averages, i.e., for the attended and the unattended target tones. Consistent with broad spread of the topography, we did not find that a single source accounted for the frontal topography. In order to examine which regions of prefrontal cortex could account for the data, we seeded our first model with three regional dipoles, one each in the midline dorsal, rostral and ventral/subgenual anterior cingulate. These models accounted for 86% and 88% of the variance in activity to attended and unattended tones. Expanding these to symmetric pairs still within the midline tissue improved the model to 94% of the overall variance. Including lateral sites did not improve the model. Thus, this minimal success requiring a great many frontally placed dipoles suggests that the positivity at the scalp is
not due to a small number of generators. This is consistent with the spread of the signal at the scalp both spatially and temporally.

Discussion

The goal of the present study was two-fold. First, we wished to examine the EFP and N1 elicited during a selective auditory attention task in typically developing adolescents in order to better understand the response in adolescence of each of these components and their respective modulation by selective attention. Stevens and colleagues (Coch et al., 2005; Stevens et al., 2008; Stevens et al., 2009; Stevens et al., 2006) suggested that, at least in young children, the early ERP varies with attention, and we wished to determine whether this same pattern would emerge in our adolescent sample. Second, we wished to examine the relation between naturalistic manifestations of executive function and the EFP and N1 because of prior literature pointing to the centrality of attentional control for EF. Adolescence is an age group where EF is of particular developmental importance and such a neural correlate may shed light on disorders where both selective attention and EF are impaired (e.g., ADHD).

First, we found evidence in our adolescent sample for an early frontal positivity (EFP) associated with selective attention, considered to be an important aspect of attentional control. Taken together, Stevens et al. (2006) and Coch et al. (2005) report evidence of an attention-sensitive EFP component in 3.5 to 8.5 year olds during selective auditory attention tasks. We found evidence that this EFP remains sensitive to selective attention (particularly for those with good executive functioning) even during the adolescent period and that during this developmental period the EFP is additionally accompanied by the traditional N1 component. This is consistent with work by Johnstone et al. (1996) and Ponton et al. (2000), and suggests that N1 differentiation develops
sometime between 8 and 12 years of age. At present it is unclear if or when attentional modulation of the EFP is no longer observed. Future studies could chart the progression of each of these ERP indices of selective attention in conjunction with one another across development.

Second, we found that greater EFP amplitudes to unattended stimuli were associated with poorer EF as reported by parents on the BRIEF. EFP amplitudes were larger for unattended rather than attended stimuli in those scoring in the bottom third of the BRIEF distribution. This was additionally confirmed with an analysis of average amplitudes taken from sequential 10 ms segments of data. By approximately 95 ms, those in the top third of the distribution are able to “shut off” processing of unattended stimuli while those in the bottom third continue to process this same information. In exploratory regression analyses using continuous BRIEF scores and peak EFP amplitudes, the MI subscales Initiate, Plan/Organize, and Working Memory showed this pattern most strongly. These effects were confirmed using averaged amplitudes for the timing of the EFP. That is, larger EFPs to unattended stimuli were associated with poorer EF. None of the BRI subscales showed an association with EFP characteristics. Thus, EFP amplitudes appear to be linked to the planning and organizational aspects of EF (MI), whereas they do not appear to be associated with inhibitory aspects of this same construct (BRI), which was related to the N1 (see below). However, the magnitude of the EFP/EF associations were relatively small, with the largest effects observed when EF was assessed holistically by breaking participants down into tertials based on GEC scores.

Our research raises the important question of whether the EFP is truly a different component from what has been observed in past studies of auditory selective attention in
adults, such as the P1/P50 and the earlier midlatency components following the Na. We believe that it is not equivalent to these components for three reasons. First, although in adults the frontal P1/P50 component is sometimes elicited by standard and target tones during selective auditory attention tasks, it is not consistently modulated by attention allocation (see e.g., Picton & Hillyard, 1974; Picton, Hillyard, Krausz, & Galambos, 1974) as was our EFP. Picton et al. (1974; 1974) describe their P1/P50 as having a frontal generator (similar to our EFP), but given the lack of attentional modulation of this component we do not believe these components are the same. Second, the P1/P50 is a fast-resolving component that usually requires high-pass filtering e.g., 10-50 Hz (Dalecki, Croft, & Johnstone, 2011; Knott, Millar, & Fisher, 2009) or thousands of trials to resolve any slow wave activity (Picton & Hillyard, 1974) in order to measure it. Our EFP is a much slower waveform spread over several tens of milliseconds measured without such harsh filtering or high numbers of trials. The midlatency components, in contrast, have been shown to be sensitive to attentional demands in adults (e.g., the thalamically gated auditory cortex P20-50 attention effect seen in Ahveninen et al., 2003; Woldorff & Hillyard, 1991), but they too require hundreds of trials presented at a more rapid rate than that used in the present study in order to be elicited, and like the P50 resolve quickly. Although both the EFP and midlatency responses are scored at similar maximal frontal midline sites, their cortical sources are quite different from one another, with the EFP presently showing a distributed frontal generator and the midlatency components having a likely generator in the auditory cortex (Ahveninen et al., 2003). For these reasons, we do not believe that the EFP we have observed is the same component observed in these P1/P50 and midlatency studies.
The functional significance of the EFP is not fully understood, but given its maximal location at frontal sites and the challenge of the task, it could be related to specific aspects of supervisory functions related to the ability to suppress automatic attention to distractors. This in turn would influence the general planning and organizing of behavior. Consistent with this, patients with lesions of the frontal lobes, the likely multi-sourced generator of the EFP, show difficulties ignoring distractors, resulting in inefficient planning and monitoring of their behavior (Glosser & Goodglass, 1990). MacCoon, Wallace and Newman (2004) theorized that the suppression of dominant networks generating prepotent maladaptive behavioral response alternatives is required for self-regulated behavior. It would seem that adolescents with poor self-regulatory skill have difficulties suppressing attention to irrelevant information, at least in the auditory modality.

With respect to the N1 component, our auditory N1 was maximal at CPz, whereas it is normally maximal closer to Fz in adults (Di Russo, Martinez, & Hillyard, 2003; Singhal et al., 2002). An examination of the overlays reported by Johnstone et al. (1996) demonstrate that the N1 at Fz for young adolescents does not constitute a clear peak and seems to be obscured by some slow wave activity. This peak becomes clearer at Pz, closer to our measurement site. Thus we believe that these differences in measurement sites were appropriate to the age range of our participants. The functional significance of these topographical differences is unclear although they are consistent with developmental literature charting the late frontalization of the brain as measured during an inhibitory control task (Rubia et al., 2000). Moreover, the N1 amplitudes that we recorded in the present study were somewhat smaller (by approximately 2µV) than those
reported in Johnstone et al. (1996). These differences in amplitude may be explained by differences in reference electrode. Whereas Johnstone et al. (1996) used linked earlobes, we used an average reference in the present study, which would of course influence voltages observed across scalp locations (Pivik et al., 1993).

Peak-scored N1 amplitudes did not relate to BRIEF scores in either continuous or extreme group approaches; however some group differences were noted at later latencies using the averaged amplitude values. Averaged amplitude values at Cz and CPz differed as a function of attention in the bottom third group only (most robust overlap at the two sites from 175 - 225 ms). This effect was later than the peak of the N1 (which occurs between 125 and 165 ms), and later than the EFP attention effect found in the top third group (from 95 - 125 ms). Thus, while poor self-regulators do successfully differentiate attended and unattended tones, this differentiation occurs later than the relatively rapid differentiation observed in the top-third group and this differentiation is reflected in the activation of a different ERP component.

Moreover, whereas we initially predicted that rapid processing (as indexed by shortened latencies) to behaviorally relevant stimuli (i.e., attended stimuli) would be associated with improved EF, we found that it was shortened latencies to the N1 for unattended stimuli that related to unique variance in overall GEC scores. Various follow up analyses of correlations with subscales indicated in all cases that rapid responses to unattended stimuli were associated with better self-regulatory skill. Among these subscales, N1 latencies are most strongly associated with the inhibitory aspects of EF (BRI) but not with the planning and organizational aspects of EF (MI).
Our results suggest that the ability to show a speeded neural response to an unattended stimulus (i.e., an ability to disengage attention from task irrelevant information in the early stages of stimulus processing) appears to confer some advantage for selective domains of self-regulatory skill. Thus, executive functioning skills, normally considered “top-down” processes, were related to automatic aspects of selective attention in the present study. If Singhal, Doerfling, and Fowler (2002) are correct in proposing that the N1 represents an automatic gating mechanism to further processing, it might be beneficial to begin this inhibition to unattended stimuli as quickly as possible. Thus, we can say that good self-regulators show efficient attentional control as indexed by rapid information gating. Here, we found somewhat of a dissociation between the EFP and the N1 in terms of their respective correlates with EF (i.e., correlates with MI versus BRI indices, respectively) supporting the notion that although they occur at similar time points, they reflect different underlying neural processes, a dissociation that merits further examination. We can hypothesize that the rapid gating of to-be-ignored information (as indexed by N1 latencies) is an indicator of inhibitory control in everyday behavior as indicated by the BRI scales of EF. This is consistent with clinical literature involving children with attention deficit hyperactivity disorder which documents concurrent difficulties in filtering out to-be-ignored information and poor inhibitory control (Mayes & Calhoun, 2007; Wahlstedt, 2009).

Overall, we are beginning to build a profile of an adept self-regulating adolescent as one who produces reduced frontal responses to to-be-ignored stimuli, and filters them out quickly. The precise mechanisms that underlie this effect will, of course, require further investigation. Yet, no matter what the ultimate explanation for the association between
attentional control and positive developmental outcomes, this association is likely to have developmental implications throughout adolescence. Sethi, Mischel, Aber, Shoda and Rodriguez (2000) followed a group of children as they made the transition from toddlerhood (age 12-24 months) to preschool years (age 5 years) and found that children who used the most effective strategies for directing their attention in a stressful situation were also the children who 3½ years later were able to adeptly deploy their attention in a delay-of-gratification paradigm. Eigsti et al. (2006) studied these children again some 14 years later and found that their attentional control as preschoolers in the delay-of-gratification paradigm was associated with their skill on a go/no-go task in adolescence. Thus, the ability to successfully control attention may be a developmental precursor for many important skills, including EF, and may be an important protective factor decreasing risk for clinical conditions involving disordered EF.
References


Pivik, R. T., Broughton, R. J., Coppola, R., Davidson, R. J., Fox, N., & Nuwer, M. R. (1993). Guidelines for the recording and quantitative-analysis of


3. STUDY 2

Individual differences in adolescent self-regulation are highly consequential for developmental outcomes. Like most complex behavioural phenotypes, self-regulation is multiply determined. Though they are not mutually exclusive, research points towards biological (e.g., genetic and electrophysiological) correlates and environmental (e.g., peer culture) correlates, but the complex relationships among all of these variables are not well understood. Here, we attempt to uncover the relationships among a few of these multiple predictors, namely, the relationships between genes related to the monoamine system and electrophysiological indices of frontal lobe functioning as they relate to behavioural self-regulation. Electrophysiological measures represent one possible endophenotype linking genes to self-regulation (i.e., a physiological mediator). However, full mediation of the gene – self-regulation relationship by event-related potentials (ERPs, our physiological variable of interest) is difficult to establish (see Green, Ha, & Bullock, 2010, for a discussion of the difficulties of testing mediation), but is also unlikely given the multiple sources of variance contributing to self-regulation (see e.g., Posner & Rothbart, 2000). Instead our focus is on the moderating role that genes may play in the self-regulation – ERP relationship.

**Electrophysiological Correlates of Self-Regulation**

Much of the work on the electrophysiology of self-regulation in adolescence has focused on later occurring ERP components (e.g., the P300) in clinical samples. For example, a substantial literature documents abnormalities in the novelty-P300 (an index of attentional alerting) in children with attention deficit hyperactivity disorder (ADHD) (see e.g., Gumenyuk et al., 2005), a condition hallmarked by reduced self-regulatory skill. However, Lackner et al. (2013) found that an early occurring electrophysiological
response to to-be-ignored stimuli recorded over frontal sites correlated with parent reports of their adolescent's self-regulatory skill, suggesting that these early ERPs have utility for gaining a better understanding of self-regulation. Understanding where in the information processing stream these associations emerge may help better guide treatment plans for those with disordered self-regulation.

Lackner et al. (2013) used a selective auditory attention task to assess attentional control. In this paradigm participants are presented with two types of tones – high and low pitched – in a separate, random, non-overlapping fashion to each of their ears. Participants are asked to respond to high pitched sounds (i.e., targets) in one ear only, and to ignore the other ear. In healthy adults, ERPs are larger for attended rather than unattended stimuli (the N1d effect). Electrocortical responses to unattended targets can be used as a metric of the adolescent's ability to suppress to-be-ignored stimuli. An early frontal positivity (EFP) recorded at Fz and the N1 latency scored at CPz to unattended targets predicted self-regulation (Lackner et al., 2013). Here we follow up on those results.

**Genetic Correlates of Self-Regulation**

**Dopamine (DA).** Dopamine is broadly involved in psychological processes, and shows more specific associations with the functions of the frontal lobe. Physiological explanations for these results rest on the knowledge that most DA neurons originate subcortically from the ventral tegmental area (VTA) and then project forward in the brain along several different pathways, including the mesocortical tract which terminates in the dorsal-medial prefrontal cortex (dmPFC), an area both rich in DA receptors and important to regulated behaviour.
Dopamine exerts strong developmental effects. Animal studies have shown DA to influence proliferation and differentiation of precursor cells in regions of embryonic mouse telencephalon, including the PFC (Popolo, McCarthy, & Bhide, 2004) suggesting that this neurotransmitter may have important developmental effects on brain structure and function. Indeed, research from Adele Diamond and colleagues supports this assertion. These researchers have conducted many studies on children with phenylketonuria (PKU), a metabolic disorder that decreases available dopamine. These children consistently show impaired performance on tasks that are associated with frontal lobe development (see Diamond, 2001, for a review).

Moreover, a substantial literature connects allelic variants in genes related to dopamine synthesis, degradation and transport to individual differences in self-regulation and/or executive functioning, specifically the DRD4 and COMT genes.

**DRD4** is a DA receptor gene that contains a polymorphic number of amino acid sequence repeats (VNTRs ranging from 2-11) at exon 3 as well as a single nucleotide polymorphism (SNP) in the promoter region. Receptors arising from the 7-repeat VNTR are less responsive to DA than are receptors arising from the 2- or 4-repeat variants (Asghari et al., 1995). The T variant of the SNP (**DRD4** rs1800955) is associated with a reduced initiation of **DRD4** gene transcription (Okuyama et al., 2000).

The **COMT** gene codes for an enzyme which inactivates dopamine by attaching a methyl group to the molecule. This causes a consequent reduction in post-synaptic DA stimulation. Three very common haplotypes consisting of four SNPs covering the **COMT** region from intron 2 to exon 4 can be combined to determine one's **COMT** haplotype: A/G rs6269, C/T rs4633, C/G rs4818, and Val/Met rs4680. While Val/Met rs4680
frequently shows associations with complex phenotypes, these associations are often small and relatively inconsistent, leading Nackley et al. (2006) to conclude that additional SNPs are required to fully explain COMT activity. Nackley et al. found exactly this. COMT haplotypes predicted pain sensitivity better than rs4680 alone (the dopaminergic system is also related to pain; Nackley et al., 2006). Importantly, the predictive value of the COMT haplotype extends beyond pain sensitivity to the physiological level. Those with the low haplotype have the highest levels of COMT enzymatic activity, and those with the high haplotype have the lowest enzymatic activity, thus COMT haplotypes are a more comprehensive way of examining the functioning of the COMT system. These variants account for 96% of all haplotypes observed (Diatchenko et al., 2005). Therefore, we analyze COMT haplotypes rather than individual SNPs in the present study.

Previous research has connected allelic variants in each of the dopamine-related genes to performance on executive functioning tasks across development. Executive functioning skills of preschool aged children are correlated with DRD4 allele length such that a smaller number of repeats, and therefore more responsive dopamine receptors (i.e., more signalling) are associated with better executive functioning performance (Lackner, Sabbagh, Hallinan, Liu, & Holden, 2012). Moreover, several studies have linked allelic variations in both the VNTR (specifically the 7-repeat allele) and SNP (specifically the T allele) of DRD4 as well as the Val158Met SNP of COMT to ADHD (see Eisenberg et al., 1999; Lowe et al., 2004; Shaw et al., 2007). A substantial literature connects allelic variations of COMT to performance on the Wisconsin Card Sort Task (Egan et al., 2001; Lipsky et al., 2005) and psychomotor vigilance tasks in adults (Lim et al., 2012) and a directional Stroop task in children (Diamond, Briand, Fossella, & Gehlbach, 2004).
Serotonin (5-HT). Like the dopamine system, the serotonin system also projects from subcortical regions forward to areas of the brain associated with executive control. Serotonergic neurons ascend from the rostral and caudal raphe nuclei to several regions of the cerebral cortex and limbic system (Jacobs & Azmitia, 1992). Animal studies have suggested a strong role for 5-HT in key neural developments such as neurogenesis, apoptosis, axon branching and dendritogenesis, particularly within the neocortex (Gaspar, Cases, & Maroteaux, 2003; Janusonis, Glunic, & Rakic, 2004; Khozhai & Otellin, 2006), processes which continue throughout adolescence but slow down dramatically thereafter (see e.g., He & Crews, 2007).

Serotonergic signaling is largely terminated by reuptake via the serotonin transporter gene (5-HTSLC6A4). The 5-HTTLPR VNTR, a functional polymorphism in the promoter region of the serotonin transporter gene, has shown interesting psychological correlates, discussed below. The number of repeat segments has consequences for the amount of serotonin available for synaptic transmission. The short allele results in lower expression of the serotonin transporter and therefore greater quantities of available 5-HT and the long allele results in higher expression of the transporter and therefore a smaller quantity of available 5-HT.

Clinical populations where regulatory behaviour is not normative show increased incidence of the long allele (Kent et al., 2002). More specifically, 5-HT related genes have been implicated in the pathophysiology of ADHD and oppositional defiant disorder (ODD; Comings et al., 2000), suggesting an association with self-regulation in real-world contexts. Genetic variants of serotonin-related genes are also associated with cognitive self-regulation in preschool aged children and in adults (e.g., using lab based measures of
executive functioning: Anderson, Bell & Awh, 2012; Borg et al., 2009; Canli et al., 2005; Kochanska, Philibert, & Barry, 2009; Roiser, Rogers, Cook, & Sahakian, 2006), whereby the short allele is most commonly found to be linked with higher executive control. Such specific associations with self-regulation in adolescence have yet to be reported. ERPs may help provide some mechanism for these associations. For example the short allele has been previously associated with greater error-related negativities (ERNs) in an error-monitoring task, indicative of stronger performance monitoring (Fallgatter et al., 2004). The N1d effect observed in selective auditory attention tasks may be altogether absent in individuals homozygous for the long/long allele (Bell, Stevens, & Neville, 2010). Thus, allelic variants in 5-HTTLPR may be associated with both neural and behavioural measurements of regulated behaviour.

To our knowledge, no study has examined the associations between these genotypes, electrophysiological markers of frontal function, and real-world self-regulatory skill in a group of typically developing adolescents. In this study we do this with the following goals: (1) to test the hypothesis of whether monoamine genes affect self-regulation directly, or only through their effects on PFC activation (as reflected in ERPs), (2) to understand whether monoamine genes moderate the association between our electrocortical responses and self-regulation.

Methods

Participants

Participants consisted of 48 adolescents 12 to 14 years of age (21 female, mean age = 13.1 yrs). Fifty one participants successfully completed the selective auditory attention task, but we had to exclude one who had a substantial hearing loss, one with ERP amplitudes more than 2.5 standard deviations above the mean, and one with a large
number of false positive responses on the behavioral task. Participants were recruited based on their prior participation in a cardiovascular health study conducted in the Health Sciences department, Brock University. Genotyping success rates and distributions are presented in Table 2.1, and cross tabulations of allelic variants are presented in Appendix C.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Variant #1</th>
<th>Variant #2</th>
<th>Variant #3</th>
<th>Sample Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>DRD4</em> VNTR</td>
<td>7-repeat allele present (11)</td>
<td>7-repeat allele absent (32)</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td><em>DRD4</em> rs1800955</td>
<td>T allele present (38)</td>
<td>T allele absent (8)</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><em>COMT</em> haplotype</td>
<td>High haplotype present (31)</td>
<td>High haplotype absent (15)</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td><em>5-HTTLPR</em></td>
<td>High activity (10)</td>
<td>Intermediate activity (25)</td>
<td>Low activity (11)</td>
<td>2</td>
</tr>
</tbody>
</table>

**Materials**

**Selective auditory attention task.** Participants were seated in an electrically shielded room. Two digitized sounds were presented using Etymotic ear inserts (Etymotic Research Inc.). These stimuli consisted of a 1000 Hz (88% probability, nontarget) and a 2000 Hz (12% probability, target) 200 ms tones. During an initial practice block, participants were presented with an example of each type of stimulus and asked to perform 10 practice trials whereby sounds were presented with a variable interstimulus interval of 600 to 800 ms randomized across ears. Participants were instructed to attend to one ear only and to ignore all sounds presented to the other ear. While remaining visually fixated on a cross at the centre of the computer screen, they were asked to respond by pressing a number on a key pad when they heard the target tone in the
attended ear, and not to respond otherwise. Task instructions were presented in written form on the computer monitor while concurrently read aloud by a pre-recorded female voice. See Appendix B for a graphical representation of the task.

The test trials included four blocks of 200 trials each. Trial breakdown across the entire task was as follows: forty-eight 2000 Hz tones presented to the attended ear (attended targets, subsequently referred to as ATs), forty-eight 2000 Hz tones presented to the unattended ear (unattended targets, subsequently referred to as UTs), three-hundred and fifty-two 1000 Hz tones presented to the attended ear (attended non-targets), and three-hundred and fifty-two 1000 Hz tones presented to the unattended ear (unattended non-targets). After the completion of each 200-trial block, there was a 20-second break and participants were then asked to switch their ear of attention and to respond to target tones in that ear only. All participants began the task attending to their right ear. The task took approximately 15 minutes to complete and was part of a larger study on adolescent development.

Here we also analyze performance data from the task including the number of attended targets correctly responded to, the number of false alarms to unattended targets, and the average reaction time to correctly responded-to targets. These measures can be also used as a proxy for self-regulation, as considerable goal directed behaviour, inhibitory control, sustained attention, and selective attention are required to complete this task.

Adolescent Self-Regulation Inventory (ASRI; Moilanen, 2007). The ASRI is a 28 item self-report questionnaire that asks adolescents to evaluate their naturally-occurring self-regulatory abilities. We subdivided the questions and summed their
responses to form two subscales: a cognitive ($\alpha = .83$) and emotional ($\alpha = .55$) self-regulation score along with an overall self-regulation score. Higher scores represent better self-regulatory skill. Items include “If something isn’t going according to my plans, I can change my actions to try and reach my goal” (Cognitive) and “When I have a serious disagreement with someone, I can talk calmly about it without losing control” (Emotional). See Appendix A.

**Behavior Rating Inventory of Executive Function (BRIEF; Psychological Assessment Resources, Inc).** The BRIEF parent report form is an 86-item measure that asks parents to evaluate their child’s daily behavior with respect to eight domains of self-regulation. The overall Global Executive Composite (GEC) is divided into eight theoretically and empirically derived scales which are then combined to form two indices, the Behavior Regulation Index (BRI) and the Metacognition Index (MI). The BRI (subscales: Inhibit, Shift, and Emotional Control) represents the child’s ability to utilize appropriate inhibitory control in the service of shifting cognitive set, modulating emotions, and modulating behavior. The MI (subscales: Initiate, Plan/Organize, Working Memory, Organization of Materials, and Monitor) represents the child’s proficiency at self-managing tasks and self-monitoring. Scores were inverted so that higher scores represented higher levels of regulatory skill.

**Self-Administered Rating Scale for Pubertal Development (Carskadon & Acebo, 1993).** This questionnaire asks individuals to report on their physical developments associated with pubertal maturation. Boys and girls are both asked to report on changes in height, body hair, and skin complexion. Boys are additionally asked to report on any changes to their voice or facial hair. Girls are asked about breast growth
and the onset of menstruation. Higher scores represent greater levels of pubertal maturation.

Procedures

**EEG recording and data analysis.** EEG was recorded at 121 scalp sites (EGI, Eugene, OR) at a sampling rate of 500 Hz with 0.1-100 Hz analog filtering. Impedances were below 50 kΩ when recording began, and were checked throughout the session to ensure that they remained at this level. Data were re-referenced offline to the average of all sites, filtered offline (1-30 Hz) and corrected for eye movements using the Gratton and Coles procedure (Gratton, Coles, & Donchin, 1983). In addition to manual examinations of the data, trials with artifacts were automatically removed with a ±75 µV criterion, and then averaged into ERP segments of 1000 ms for target tones correctly responded to in the attended and unattended ears separately, including a 200 ms prestimulus baseline. Peak amplitudes and latencies were clearly maximal over midline sites, as is traditionally found for the N1 (Fz, FCz, Cz, CPz, Pz), with focal data analyses conducted at Fz for the EFP and CPz for the N1, sites where each component had its maximum peak amplitude.

**Genotyping parameters.** DNA was extracted from Whatman's sterile Omni Swab collection pads using standard laboratory procedures. DNA concentrations were measured by Nanodrop (ND-1000 Spectrophotometer). Genotyping was completed as follows and random duplicate samples (25%) were included to check accuracy. The error rate was <0.005, and the completion rate was >0.95. Hardy-Weinberg equilibrium (HWE) was assessed using Pearson’s chi-square method for all genotypes.

---

Of the 128 channels available, 7 were used for physiological records (heart rate, respiration, etc.) and are not reported here leaving 121 for EEG recordings.
**COMT haplotype.** rs6269, rs4633, rs4818, rs4680 (Val158Met) SNPs were obtained as a Taqman Assay (C___2538746_1_, C___2538747_20, C___2538750_10, C_25746809_50, respectively; Applied Biosystems, Foster City, USA). Each TaqMan assay was amplified from 10 ng genomic DNA. Genotyping was performed according to the manufacturer’s protocol. For each reaction the following volumes of reagents were used: 2.5 µl of 2X Universal PCR Master Mix (PN 4304437), 0.25 µl of each SNP assay in a total reaction volume of 5 µl. Amplifications were performed on a Perkin-Elmer 9700 thermocycler (Applied Biosystems, Foster City, CA, USA) with one cycle at 95°C for 10 min followed by 50 cycles of 92°C for 15 s, 60°C for 90 s.

The genotype was determined at end-point using ABI 7900HT Sequence Detection System (SDS) software. Following Nackley et al., (2006) participants were categorized as possessing one of three genotypes – low, medium or high. rs6269, rs4633, rs4818 and rs4680 produce a combination of SNPs with the following designation: GCGGval (LPS), ATCAmet(APS) and ACCGval(HPS) haplotypes. Following Fijal et al. (2010) we then grouped together those who possessed at least one LPS allele and compared them to those without the LPS (APS and HPS) allele in order to maximize power. For clarity, throughout this dissertation we will refer to those with at least one LPS allele as belonging to the high allele present group (high in this case refers to the levels of COMT enzymatic activity) and those without an LPS allele as belonging to the high allele absent group (therefore lower COMT enzymatic activity).

**DRD4 VNTR.** The DRD4 48 basepair VNTR polymorphism at exon 3, chromosome 11, was amplified from 20 ng genomic DNA using the primer sequences:
forward 5’-(GACCGCGACTACGTGGTCTACTC)-3’ and reverse-
5’(CTCTTGCAGCTTCGCCGCCAG)-3’ (Monuteaux et al., 2008).
Owing to the high GC content in the VNTR region, amplification was performed using
GC-Rich PCR System (Roche Applied Science, 68298 Mannheim, Germany). The PCR
conditions were for initial denaturation 95°C (3 min), 10 cycles of 95°C (30 s), 60.5 °C
(35 s), 72°C (45 s), and 25 cycles of 95°C (30 s), 60.5 °C (35 s), 72°C (45 s +5 s for each
cycle in addition), and a final elongation, 72°C (10 min). The forward primer was labeled
with the fluorescent dye 6-FAM, amplicons were visualized with GeneScan-1200 LIZ
Size Standard (Applied Biosystems, Foster City, CA, USA) and analyzed on an ABI
3730 capillary sequencer. Allele sizes (allele 2, 404bp; allele 3, 452bp; allele 4, 500bp;
allele 5, 548bp; allele 6, 596bp; allele 7, 642bp; allele 8, 692bp; allele 9, 740bp; allele 10,
785bp; allele 11, 836bp) were determined using GeneMapper v4.0 (Applied Biosystems,
Foster City, CA, USA). Following Auerbach et al. (2001) and Biehl et al. (2011) we
grouped participants based on the presence or absence of a 7-repeat (risk) allele.

**DRD4 rs1800955.** rs1800955 SNP T521C was obtained as a Taqman assay
(C__74707000_30; Applied Biosystems, Foster City USA) and was determined using
the forward primer 5’-GGCGGCCACGCGAGGATCAACTGTGC-3’ and the reverse
primer 5’-CGGCCAGACCAGGCCCCTGAGC-3’. Given the T allele's association with
ADHD, participants were categorized as either possessing or not possessing the risk
allele (T) following Eichhammer et al. (2005).

**5-HTTLPR.** Genotyping of the SLC6A4 promoter (5-HTTLPR) was
accomplished in two stages using size discrimination accompanied by MspI restriction
enzyme digestion for SNP rs25531. The 5-HTTLPR region was PCR amplified with the
primers: ATCGCTCCTGCATCCCCCATTAT (forward), and
GAGGTGCAGGGGGATGCTGGAA (reverse). The reverse primer was FAM-labeled.
PCR was performed in a 20µl reaction containing 10ng genomic DNA, 1x Optimized
buffer A, 1x PCR enhancer, 0.25µM PCR primers (each primer), 0.125µM dNTP, 1.25
units Platinum Taq polymerase (all Invitrogen Corp., Carlsbad, CA), using the
amplification conditions on a Perkin-Elmer 9700 thermocycler (Applied Biosystems,
Foster City, CA, USA) of: 95°C (5 min), 40 cycles of 94°C (30 s), 52 °C (30 s), 68°C (1
min), followed by a final elongation step of 68°C (10 min). For distinguishing the S and
L alleles, 2µl of the PCR reaction mix was added to 8µl loading mix (7.5µl formamide,
0.5µl GeneScan™-500 ROX Size Standard (Applied Biosystems, Foster City, CA).

For genotyping rs25531 (the A/G substitution in the L allele), 5µl of the PCR
mix was added to a 5µl restriction digest mix, containing 100,000 U/ml MspI, 10x NE
restriction buffer 4 (New England Biolabs), incubated at 37°C for 1 hour, and 2µl of
reaction mix added to 8µl loading mix (see above). Allelic discrimination for S (103bp)
and L (146bp) alleles, and for L_A (146bp) and L_C (85bp) post-digestion alleles was
performed by size determination on a 3730 DNA Analyzer, data analyzed using
GeneMapper 4.0 software (Applied Biosystems).

As is traditionally done, participants were categorized as having low (SS, SLG,
LGLG), intermediate (LALG, SLA) or high (LALA) activity 5-HTTLPR alleles. Those
with the high activity, or long 5-HTTLPR VNTR, show a higher level of 5-HT transporter
expression, while those with the low activity, or short 5-HTTLPR VNTR show a reduced
level of transporter expression.
### Table 2.2. Genetic risk summary table

<table>
<thead>
<tr>
<th>Gene</th>
<th>Neurotransmitter system</th>
<th>Low-risk variant</th>
<th>High-risk variant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRD4 VNTR</strong></td>
<td>Dopamine</td>
<td>7-repeat allele absent</td>
<td>7-repeat allele present</td>
</tr>
<tr>
<td><strong>DRD4 rs1800955</strong></td>
<td>Dopamine</td>
<td>T allele absent</td>
<td>T allele present</td>
</tr>
<tr>
<td><strong>COMT haplotype</strong></td>
<td>Dopamine</td>
<td>High haplotype absent$^t$</td>
<td>High haplotype present$^t$</td>
</tr>
<tr>
<td><strong>5-HTTLPR</strong></td>
<td>Serotonin</td>
<td>Low activity</td>
<td>High activity</td>
</tr>
</tbody>
</table>

Note: COMT haplotypes have not been extensively investigated for their association with risk of psychopathology, and so the high versus low risk designation here needs further validation. The high haplotype present group would have higher COMT enzymatic activity, and therefore lower levels of dopamine in PFC, a condition which has previously been associated with risk for psychopathology.

### ERP Analysis

Using permutation-based statistics implemented in EEGLAB, we looked for condition (AT vs UT) and group (genotype) differences in ERPs (specifically the EFP and N1 from 30 - 215 ms post stimulus) recorded at our two focal sites of interest – Fz and CPz.

The goal of permutation tests is to test the null hypothesis that the groups (or conditions) have identical distributions (Wilcox, 2005). These distributions are empirically, rather than theoretically, derived. In EEGLAB we calculated the difference between the sample means ($d$) at every datapoint and calculated a distribution of randomly shuffled difference scores across the pooled data. If the null hypothesis is true, then the order of the observations is arbitrary. For instance, if at 20 ms a participant has an average ERP response of 1µV to attended targets, and .5µV to unattended targets, they are just as likely to have had .5µV ERP to attended targets and 1µV to unattended targets if the null hypothesis of no condition differences is assumed. When testing within-subjects effects (i.e., AT UT effects within a particular genotype), within each genetic
group, subject-averaged ERP amplitudes were reshuffled and difference scores calculated 2000 times (permutations). The values were sorted in ascending order to create a distribution of differences. If our original sample mean lies in the tail of this surrogate value distribution, then the null hypothesis of no difference between conditions is rejected for that datapoint. This is repeated for every datapoint of the ERP. When testing for between-subjects effects the identical procedure is followed, except that ERP amplitudes are pooled across a condition (e.g., all AT amplitudes are pooled) rather than across groups.

Two theoretical issues regarding the data analytic approach taken here need to be addressed. Firstly, Bonferroni and Šidák corrections are frequently used to combat the problem of multiple comparisons, but are regarded as overly conservative (Bland & Altman, 2005). Less conservative statistical tests can be used to address the issue of multiple comparisons (e.g., Tukeys and REGWQ) but they too depend crucially on the assumption of a normal distribution (Kesselman, Cribbie, & Holland, 2004). Permutation tests have been successfully used in their place to keep alpha at the nominal level (Conneely & Boehnke, 2007; Kesselman, Cribbie, & Holland, 2004; Maris & Oostenveld, 2007), but permutation tests likewise assume the groups have equal variances (Wilcox, 2005). The current data analytic approach controls for multiple comparisons by using permutation based statistics. Because each data point has its own set of associated test statistics and reporting all of them would be cumbersome, they are not reported here. Instead we present $p$ values as graphical representations of observed differences between conditions and/or genotypes.
Genes and Self-Regulation

In order to determine whether the genetic groups differed on self-regulatory skill as indexed by the BRIEF, ASRI and performance on the auditory attention task we performed a series of one-way ANOVAs using a bootstrap $t$-method in R, with 10% trimming and 2000 bootstrap samples. Extensive details on this method can be found in Chapter 7 of Wilcox (2005).

Because both age and pubertal status are theoretically related to self-regulation, we first predicted each of our self-regulatory variables by age and pubertal development using linear regression and saved the standardized residuals. These standardized residuals were used in all subsequent analyses.

Moderation Analysis

As stated in the introduction, we wanted to know more about individual differences contributing to the association between self-regulation and ERPs related to attentional control. To do this we performed a moderator analysis using robust statistics implemented in R. Specifically, we utilized Rand Wilcox's `reg2ci` function (Wilcox, 2005) to see if the slope of the association between our ERP measures and self-regulatory variables differed as a function of genotype. If the groups show significantly different slopes we can assume a moderating role of genes. The `reg2ci` function computes the .95 confidence interval for the differences between regression slopes using the Theil-Sen estimator (a robust regression estimator with demonstrated success in small samples) and 2000 bootstrap samples (Wilcox, 2005). Ninety five percent confidence intervals around the slopes of the relationships for individual genotypic groups were calculated with the
tshdreg function and 2000 bootstrap samples (Wilcox, 2005). In these analyses we utilized the peak scored amplitudes and latencies from Lackner et al. (2013).

**Results**

**Genes and ERPs**

The first step of demonstrating a moderating role for monoamine related genes on self-regulation and selective-auditory attention ERPs is to establish the zero-order associations between genes and each of our two dependent variables (AT and UT ERPs). Below we focus on group differences in EFPs and N1s at Fz and CPz respectively using the methods described in the section titled "ERP analysis" above. We do not discuss observed effects after this time window for a few reasons: (1) we are following up on Lackner et al. (2013) who found self-regulation-ERP associations at early rather than later time windows (this reduced focus may help us reduce our chances of Type I error) and (2) effects at later time points are not the focus of the current investigation based on the current goals and research questions.

**DRD4 VNTR.** As can be seen in Figure 2.1 (panel i), EFP amplitudes at Fz differed as a function of a significant genotype x condition interaction. Those participants with the 7-repeat allele did not differentiate between AT and UT conditions (panel c), while those without a 7-repeat allele had larger early EFPs to ATs than UTs (panel f). The 7-repeat absent group had amplified AT EFPs relative to the 7-repeat present group (panel g), but no group differences were observed to UTs (panel h). As depicted in Figure 2.2, an analysis of N1 amplitudes at CPz did not yield such a genotype x condition interaction, although N1s to attended targets were larger (i.e., more negative) in those with the 7-repeat allele in comparison to those without a 7-repeat allele (panel g).
genotype groups differentiated AT and UT conditions at the timing of the N1 (panels c and f).

Figure 2.1. DRD4 VNTR differences in the EFP at Fz. The EFP timing is highlighted by a black rectangle on each panel. Panel i depicts a significant genotype x condition interaction on EFP amplitudes. The colourbars show p values for all datapoints where robust condition or group effects were tested. Darker colours represent more highly significant effects, while light grey indicates non significant effects. All statistically significant effects are indicated by red hash marks at the bottom of the colourbar. This notation is consistent across all ERP figures.
Figure 2.2. *DRD4* VNTR differences in the N1 at CPz. The N1 timing is highlighted by a black rectangle on each panel. Panels c and f show that both groups differentiated stimulus conditions during the N1 and panel g shows that the groups differed in the size of the N1 to ATs.

**DRD4 rs1800955.** Neither genotypic group distinguished between AT and UT stimuli at the timing of the EFP at Fz (see Figure 2.3, panels c and f). However, those with at least one T allele showed larger EFPs to UT stimuli than those without a T allele (Figure 2.3, panel h). At the timing of the N1 at CPz (Figure 2.4), those with at least one T allele differentiated between conditions across the entire N1, while those without a T allele showed less persistent condition differences (panels c and f). Thus, those with a T
allele do not begin differentiating AT and UT stimuli at the timing of the EFP (Figure 2.3 panel f), but show differentiation during the timing of the N1 (Figure 2.4 panel f). Those without a T allele show a reduced EFP to UT stimuli (Figure 2.3, panel h) and a reduced differentiation during the N1 compared to those with a T allele (Figure 2.4 panels c versus f). Therefore, the groups differ in the timing and duration of their stimulus differentiation.

Figure 2.3. DRD4 rs1800955 differences in the EFP at Fz. The EFP timing is highlighted by a black rectangle on each panel. Panel h depicts group differences in UT amplitudes during the EFP.
Figure 2.4. DRD4 rs1800955 differences in the N1 at CPz. The N1 timing is highlighted by a black rectangle on each panel. Panels c and f show that both groups differentiate stimulus conditions during the N1.

**COMT haplotype.** Those with a high haplotype did not differentiate ATs and UTs at Fz during the EFP, while those without a high haplotype had more positive AT than UT EFPs in the expected direction (see Figure 2.5 panels c and f). The group difference is likely owing to larger EFPs to ATs in the high haplotype absent group (panel g). These effects were documented by a significant genotype x group interaction (panel i). As seen in Figure 2.6, both high and no-high groups had more negative N1s to AT than UT stimuli (panels c and f), but no other significant effects were found.
Figure 2.5. COMT haplotype differences in the EFP at Fz. The EFP timing is highlighted by a black rectangle on each panel. Panel i shows a significant genotype x condition interaction on EFP amplitudes.
Figure 2.6. COMT haplotype differences in the N1 at CPz. The N1 timing is highlighted by a black rectangle on each panel. Panels c and f show that both groups differentiated AT and UT stimuli during the N1.

5-HTTLPR. High, intermediate and low activity groups did not differ in their processing of AT and UT stimuli at Fz during the EFP. See Figure 2.7, panels j and k. As shown in Figure 2.8, all three groups showed the expected difference in N1 processing at CPz, but these effects did not differ substantially by group (panels c, f and i).
Figure 2.7. 5-HTTLPR differences in the EFP at Fz. The EFP timing is highlighted by a black rectangle on each panel.
Figure 2.8. 5-HTTLPR differences in the N1 at CPz. The N1 timing is highlighted by a black rectangle on each panel. All three genotype groups had larger N1s to AT than to UT stimuli, see panels c, f and i.

**Genes and Self-Regulation**

Bootstrap $t$ one-way ANOVAs were used to examine genotypic differences in self-regulatory skill as measured by parent-report BRIEF subscale scores, self-report ASRI scores, and performance on the auditory task.

**DRD4 VNTR.** Contrary to expectation, those participants with the 7-repeat allele scored higher than those without a 7-repeat allele on the BRIEF Emotional Control...
subscale \((p = .021)\). No significant differences were found on any other metric of self-regulation.

**DRD4 rs1800955.** Participants without a T allele had better BRIEF Plan/Organize \((p < .001)\), BRIEF Initiate \((p < .001)\), and BRIEF MI \((p = .01)\) scores than those participants with a T allele. Conversely, those without a T allele made fewer correct responses during the selective auditory attention task \((p = .03)\).

**COMT haplotype.** There was a trend for those without the high COMT haplotype to show better cognitive self-regulation (as measured by the ASRI) than those with the high haplotype \((p = .06)\).

**5-HTTLPR.** Those with the high, medium and low activity alleles showed marginally significant differences in their BRIEF Organization of Materials subscale scores \((p = .06)\). Follow-up pairwise comparisons showed that the low activity group had poorer self-regulation skills in this domain than either the intermediate \((p = .04)\) or high activity group \((p = .02)\).

**Model Test**

One of the main goals of the present paper was to examine whether monoamine genes moderate the association between self-regulation and PFC activation (as indexed by ERPs). Thus far we have demonstrated that (a) some ERP components recorded over frontal sites are correlated with individual differences in SR (see Study 1, published as Lackner et al., 2013), (b) polymorphisms of monoamine-related genes are related to these same ERP components (see Genes and ERPs above), and (c) monoamine genes affect some aspects of self-regulation (see Genes and Self-Regulation above). To test our model, we used Rand Wilcox’s reg2ci function in R, described in the Methods section.
We included here only those electrophysiological variables with demonstrated associations to self-regulation in our earlier study (Study 1 in this dissertation), namely the EFP amplitude at Fz to UT, and the N1 latency at CPz to UT. If the slopes of the relationships between self-regulation and ERPs of two genotypic groups are significantly different from one another then we can infer moderation.

**DRD4 VNTR, the EFP and self-regulation.** DRD4 VNTR length did not moderate the association between the EFP UT amplitudes and any of our self-regulatory variables as measured by the BRIEF and ASRI.

**DRD4 VNTR, the N1 and self-regulation.** DRD4 VNTR status showed a trend towards moderating the association between N1 UT latencies and both ASRI Cognitive and Total scores \((p = .07\) and \(p = .09\), respectively) as well as BRIEF BRI and GEC scores \((p = .08\) and \(p = .06\), respectively). DRD4 allele length significantly moderated the associations between N1 latencies and BRIEF Initiate scores, BRIEF Working Memory scores, and BRIEF MI Scores (all \(ps < .05\)). Across all of these metrics of self-regulation, for those with the 7-repeat DRD4 allele, lower self-regulation scores were associated with increased N1 UT latencies. For those without the 7-repeat allele, lower self-regulation scores were associated with reduced N1 UT latencies. See Table 2.3 for slopes and confidence intervals.

**DRD4 rs1800955, the EFP and self-regulation.** The association between the BRIEF Organization of Materials subscale and EFP UT amplitudes was nearly moderated by DRD4 rs1800955 SNPs \((p = .09\). Self-regulation scores increased as EFP amplitudes decreased in those with the T allele. In those without a T allele the opposite appeared to be true. See Table 2.4 for slopes and confidence intervals.
**DRD4 rs1800955, the N1 and self-regulation.** None of the associations between self-regulatory variables and N1 UT latencies were moderated by DRD4 rs1800955 status.

**COMT haplotype, the EFP and self-regulation.** The associations between the BRIEF Shift subscale, the BRIEF BRI scale and the BRIEF GEC scale with UT EFP amplitudes were moderated by COMT haplotype status ($p_s < .05$). Across all three of these SR measures, a negative association between UT amplitude and self-regulation scores was found in those individuals without the high haplotype. That is, more positive EFP UT amplitudes were associated with poorer self-regulatory skill. Those with the high haplotype showed no such associations.

**COMT haplotype, the N1 and self-regulation.** The moderating effect of the COMT haplotype was also observed when examining the relationship between N1 UT latency and self-regulation variables, namely ASRI Cognitive, Emotional and Total scores ($p_s < .04$) as well as BRIEF Working Memory scores ($p = .03$). Across all three ASRI measures, those with the high COMT haplotype showed a positive correlation between N1 latencies and self-regulation. That is, rapid N1 UT latencies were associated with poor self-regulation scores in this group. This pattern was not observed in those without the high haplotype. On the BRIEF Working Memory subscale, this pattern was somewhat different. Those individuals with the high haplotype showed a negative correlation between N1 latencies and Working Memory scores. Rapid N1s to unattended stimuli were associated with increased working memory skill.
Table 2.3. Genetic Moderation of the Association between Self-Regulation and the N1 UT Latency

<table>
<thead>
<tr>
<th>Self-regulation measure</th>
<th>Gene</th>
<th>Allelic variant</th>
<th>Slope</th>
<th>Lower bound CI of slope</th>
<th>Upper bound CI of slope</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRIEF Initiate</td>
<td>DRD4 VNTR</td>
<td>7-repeat present</td>
<td>11.94</td>
<td>-2.82</td>
<td>27.88</td>
<td>.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7-repeat absent</td>
<td>-7.15</td>
<td>-16.29</td>
<td>.44</td>
<td>.07</td>
</tr>
<tr>
<td>BRIEF Working Memory</td>
<td>DRD4 VNTR</td>
<td>7-repeat present</td>
<td>10.30</td>
<td>-5.02</td>
<td>24.99</td>
<td>.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7-repeat absent</td>
<td>-9.80</td>
<td>-21.31</td>
<td>-.35</td>
<td>.04</td>
</tr>
<tr>
<td>BRIEF Metacognition Index</td>
<td>DRD4 VNTR</td>
<td>7-repeat present</td>
<td>12.33</td>
<td>-5.90</td>
<td>24.96</td>
<td>.24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7-repeat absent</td>
<td>-7.24</td>
<td>-17.96</td>
<td>-.81</td>
<td>.02</td>
</tr>
<tr>
<td>ASRI Cognitive</td>
<td>COMT haplotype</td>
<td>High present</td>
<td>8.56</td>
<td>-1.39</td>
<td>21.90</td>
<td>.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High absent</td>
<td>-7.15</td>
<td>-18.67</td>
<td>-3.04</td>
<td>.007</td>
</tr>
<tr>
<td>ASRI Emotional</td>
<td>COMT haplotype</td>
<td>High present</td>
<td>11.27</td>
<td>-1.7234</td>
<td>22.03</td>
<td>.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High absent</td>
<td>-3.90</td>
<td>-11.83</td>
<td>1.04</td>
<td>.12</td>
</tr>
<tr>
<td>ASRI Total</td>
<td>COMT haplotype</td>
<td>High present</td>
<td>10.29</td>
<td>-2.71</td>
<td>20.93</td>
<td>.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High absent</td>
<td>-7.38</td>
<td>-17.70</td>
<td>2.02</td>
<td>.10</td>
</tr>
<tr>
<td>BRIEF Working Memory</td>
<td>COMT haplotype</td>
<td>High present</td>
<td>-12.23</td>
<td>-23.26</td>
<td>-2.83</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High absent</td>
<td>0</td>
<td>-6.289</td>
<td>19.39</td>
<td>.83</td>
</tr>
</tbody>
</table>

Note: Confidence intervals around the slopes of each genotypic group’s correlations were calculated using Wilcox’s function tshdreg using a Theil-Sen estimator and 2000 bootstrap samples. p values indicate whether the slope is significantly different from zero, and are different from the p values reported in text which instead represent tests of group slope differences.

**5-HTTLPR, the EFP and self-regulation.** 5-HTTLPR status moderated the associations between self-regulation and electrophysiology only slightly. Those with the
intermediate activity 5-HTTLPR allele showed a negative association between EFP amplitudes and BRIEF Inhibit scores \( (p = .05) \). That is, lower amplitude EFPs were associated with better inhibitory control in this group. The other two genotype groups did not show such an association. See Table 2.4 for slopes.

**5-HTTLPR, the N1 and self-regulation.** 5-HTTLPR status did not moderate the associations between N1 latency and any of our self-regulation variables.

### Table 2.4. Genetic Moderation of the Association between Self-Regulation and the EFP UT Amplitudes

<table>
<thead>
<tr>
<th>Self-regulation measure</th>
<th>Gene</th>
<th>Allelic variant</th>
<th>Slope</th>
<th>Lower bound CI of slope</th>
<th>Upper bound CI of slope</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRIEF Shift</td>
<td>COMT haplotype</td>
<td>High present</td>
<td>.26</td>
<td>-.27</td>
<td>1.10</td>
<td>.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High absent</td>
<td>-.61</td>
<td>-1.66</td>
<td>-.02</td>
<td>.05</td>
</tr>
<tr>
<td>BRIEF Behavior</td>
<td>COMT haplotype</td>
<td>High present</td>
<td>-.15</td>
<td>-.72</td>
<td>.39</td>
<td>.60</td>
</tr>
<tr>
<td>Regulation Index</td>
<td></td>
<td>High absent</td>
<td>-1.26</td>
<td>-2.34</td>
<td>-.47</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BRIEF Global</td>
<td>COMT haplotype</td>
<td>High present</td>
<td>0</td>
<td>-.52</td>
<td>.57</td>
<td>.97</td>
</tr>
<tr>
<td>Executive Composite</td>
<td></td>
<td>High absent</td>
<td>-1.09</td>
<td>-2.04</td>
<td>-.41</td>
<td>.006</td>
</tr>
<tr>
<td>BRIEF Inhibit</td>
<td>5-HTTLPR</td>
<td>Low</td>
<td>.20</td>
<td>-.36</td>
<td>2.85</td>
<td>.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intermediate</td>
<td>-.62</td>
<td>-1.34</td>
<td>-.003</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High</td>
<td>.24</td>
<td>-5.85</td>
<td>1.46</td>
<td>.81</td>
</tr>
</tbody>
</table>

Note: Confidence intervals around the slopes of each genotypic group’s correlations were calculated using Wilcox’s function tshdreg using a Theil-Sen estimator and 2000 bootstrap samples. \( p \) values indicate whether the slope is significantly different from zero.

**Follow-up analyses.** Related to the goals of the moderator analyses described above, we also wanted to understand whether the variance contributed to self-regulation by monoamine-related genes was independent of the shared variance between self-
regulation and the electrocortical responses of interest. To this end, we ran a robust regression procedure entering both allelic variations and ERPs simultaneously predicting our self-regulatory variables. These analyses were run only on those sets of variables for which allelic variations moderated the relationship between self-regulation and ERPs above. In only one case were genetic variants significantly independently predictive of self-regulation variables. \textit{DRD4} VNTR allele length, independent of N1 UT latencies, predicted BRIEF Emotional Control subscale scores. A follow-up regression showed that \textit{DRD4} allele length, independent of BRIEF Emotional Control scores, did not predict N1 UT latencies. All other regressions showed that the predictive value of genes and ERPs on self-regulation was overlapping.

**Discussion**

Adolescent self-regulation is multiply determined. As has been documented here and elsewhere, allelic variants in monoamine-related genes are significantly predictive of self-regulatory skill and electrocortical functioning. Genes, with their presumed ability to influence both self-regulation and ERPs may moderate the association between these two variables (complete mediation is unlikely given their multiple predictors). We made significant strides in understanding the associations between these variables.

Firstly, we found genetic effects on electrocortical responses (namely the EFP and N1) recorded during a selective auditory attention task. Participants with the \textit{DRD4} 7-repeat (risk for ADHD) allele did not differentiate between AT and UT stimuli during the EFP, while those without the risk allele did differentiate. Those with the \textit{DRD4} rs1800955 T (risk) allele showed larger EFPs to UT stimuli than those without the risk allele, and finally, those with the high \textit{COMT} enzymatic activity haplotype did not
differentiate AT and UT stimuli during the EFP as those without the high activity haplotype did. These effects all point to a dopaminergic gene effect on the EFP. Such associations were not observed for the serotonin transporter gene, suggesting some level of neurochemical specificity.

Turning to the traditionally observed N1, genetic effects were also documented. Contrary to the above, participants with the risk-associated 7-repeat allele showed larger N1s to ATs than those without the 7-repeat allele. If this N1 effect were replicated in a population with ADHD, we would be able to conclude that ADHD is not related to an overall reduced attention response, but to increased orienting to stimuli, including ATs (i.e., stimulus-driven attention rather than goal-driven attention). The N1 latency and self-regulation association in Lackner et al. (2013) was somewhat unexpected, but here we show that this association is really only true for specific genotypic groups. For example, adolescents with the high COMT enzymatic activity haplotype showed a positive correlation between N1 latencies and BRIEF Working Memory scores, but this association was not observed for those without the high COMT haplotype. These earlier and somewhat surprising effects may have been driven by one genotypic group.

However, most of our findings are consistent with the hypothesis that those individuals who possess risk alleles for disorders involving impaired self-regulation will show reduced differentiation of AT and UT stimuli, reduced processing of AT stimuli and/or amplified processing of UT stimuli relative to their non-risk allele carrying peers. For instance, those with the DRD4 rs1800955 risk allele (T) do not differentiate the stimuli during the timing of the EFP, but do differentiate it during the timing of the N1, suggesting an impaired ability to suppress the processing of to-be-ignored stimuli during
early processing stages in those who are at an increased genetic risk for developing ADHD.

These ERP differences are generally in line with the existing literature on genotypic differences in frontal functioning. Adults who differ on DRD4 allelic status (the -1217G insertion/deletion polymorphism, not assessed here) differ significantly in the activation of the ACC, as measured by fMRI during a Flanker task (Fan, Fossella, Sommer, Wu, & Posner, 2003) and adults with the Met allele of the COMT rs4680 gene have a more efficient physiological response in prefrontal cortex during a working memory task (Egan et al., 2001). In children, allelic variants of DAT1 and DRD2 genes predict the magnitude of the error-related negativity (ERN) and error-related positivity (Pe), prefrontally generated ERPs to errors (Althaus et al., 2010; Meyer et al., 2012). In addition to selective attention, error monitoring is one component of self-regulation, however much less work has focused on genetic differences in attention-related ERPs. We have done this and the results are consistent with the trends observed in the error-monitoring research, but also consistent with one study that found administration of a dopamine antagonist prior to performing a selective auditory attention task led to a decrease in N1 amplitudes to rare non-target stimuli in children with autism (Oades, Stern, Walker, Clark, & Kapoor, 1990). Essentially, reduced dopaminergic signalling led to decreased processing of novel sounds. We found that participants who have the genetic variant coding for less-responsive dopamine D4 receptors were less able to suppress processing of irrelevant sounds, and thus had poorer electrocortical 'self-regulation'.

We did not find evidence for ERP differences as a function of 5-HTTLPR allele length, despite prior research indicating that the short allele is associated with greater
ERNs in an error-monitoring task, (Fallgatter et al., 2004) and the reduction or absence of the N1d effect in individuals homozygous for the long/long allele (Bell et al., 2010). However, another line of research suggests that serotonin is particularly influential to the functioning of the anterior prefrontal cortex (Kunisato et al., 2011; Mann et al., 2000; Nakamura, Sekine, Ouchi, & et al., 2010). In our previous study (Study 1 in this dissertation) we attempted to source-localize our auditory effects, but were unable to find a precise generator. It could be that the auditory selective attention task does not rely on anterior PFC, but involves many generators, therefore decreasing the likelihood of finding serotonergic effects.

Thus, auditory selective attention appears to be more influenced by individual differences in dopaminergic rather than serotonergic functioning. Our first goal of this paper was to understand if genes influence self-regulation directly, and although the effects are small, this conclusion does seem to be warranted.

Secondly, genetic variants predicted individual differences in self- and parent-report self-regulation, and performance on the auditory task. DRD4 rs1800955 status predicted scores on several BRIEF subscales. In line with studies documenting an association between the DRD4 rs1800955 T allele and risk for ADHD (e.g., Lowe et al., 2004), those with the CC genotype showed better self-regulation than those with at least one T allele. However, contrary to expectation, those with the 7-repeat (or long) DRD4 risk allele showed higher scores on the BRIEF Emotional Control subscale and made more correct responses on the auditory task than those without the risk allele. This points to at least some subdivision of functions associated with self-regulation, and hints at the complexity of genotype-phenotype associations. In some studies, children with ADHD
and the 7-repeat allele performed better on tasks requiring self-regulatory skill than their counterparts with ADHD but without the 7-repeat allele (Bellgrove et al., 2005). Thus while the majority of the evidence suggests that possession of the 7-repeat allele is associated with poorer self-regulation, a smaller body of evidence suggests that it may be associated with better self-regulation in some contexts. This may help to explain our conflicting findings, and fits with the recently forwarded view of allelic variations as contributing to plasticity for exogenous and endogenous influences rather than as a direct marker of risk (Belsky et al., 2009; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2011).

Moreover, genetic variation in the COMT haplotype predicted self-reported self-regulatory ability. There was a trend for those without the high COMT enzymatic activity haplotype to show better cognitive self-regulation. The cognitive correlates of the COMT haplotype are not very well understood, but given the explanatory power of the COMT haplotype over single SNPs it seems important to explore these associations further. The Val/Met SNP at COMT rs4680 is one contributor to COMT haplotype status. Those with the Met/Met variant of COMT rs4680 perform better than those without the Met/Met variant on tasks of self-regulation and executive function (Diamond et al., 2004; Egan et al., 2001; Lipsky et al., 2005). The Met allele contributes to having a medium COMT haplotype status, and therefore moderate amounts of COMT enzymatic activity. This is in accord with our finding that those without the high COMT enzymatic activity haplotype show better cognitive self-regulation.

The high-activity 5-HTTLPR allele has been associated with clinical self-regulation difficulties (Kent et al., 2002), and the low-activity allele has been associated
with greater performance monitoring (Fallgatter et al., 2004) and greater differentiation of stimulus types in an auditory selective attention task (Bell et al., 2010), which may lead to the conclusion that the high-activity allele should be considered the risk allele. However, we found that the low-activity genotype group (therefore, those with the lowest serotonin transport) had poorer parent-report organizational skills than their medium- or high-activity peers. Our results are consistent with Luciana et al. (1998) who report that pharmacologically-induced increased serotonin levels are associated with impaired working memory, one subcomponent of executive functioning. Conflicting findings such as these may be explained by the potent interaction of the dopamine and serotonin systems (Di Matteo, Di Giovanni, Pierucci, & Esposito, 2008; Esposito, Di Matteo, & Di Giovanni, 2008). We were unable to test such interactions given our relatively small sample size.

Intriguingly, the associations between self-regulation and selective auditory attention ERPs were moderated by genotype. Thus, the magnitude of the association between ERPs and self-regulation was affected by genotype. For those participants with at least one 7-repeat (risk) DRD4 allele, increased N1 UT latencies were associated with poorer-self regulation, but this was not the case for those who possessed two short alleles. DRD4 rs1800955 SNPs nearly moderated the association between self-regulation and EFP amplitudes to UTs. In those with at least one risk (T) allele, a likely adaptive reduction in the size of the EFP to UTs was associated with better self-regulatory scores. COMT haplotype status also moderated the associations between self-regulation and EFP amplitudes. The medium or low haplotype group showed a negative correlation between EFP UT amplitude and self-regulation. For some genes investigated, the effects of allelic
variation on self-regulation only seemed to be indirect, i.e., there was no main effect of the gene on self-regulation, but a significant moderation of the self-regulation/ERP effects by that gene (e.g., \textit{DRD4} VNTR showed little association with self-regulation, but the self-regulation/N1 latency association was moderated by \textit{DRD4} length).

In the context of our model we can infer that \textit{DRD4} and \textit{COMT} status impact ERPs associated with selective auditory attention (our endophenotype) and self-regulatory skill. Given our design we cannot conclude causation, but only infer this as a potential explanation for our findings. Longitudinal studies are required to more fully understand the causal associations between these variables.

\textbf{Limitations and future directions.} In the present study, associations between allelic variations and self-regulation did not extend to all measures of self-regulation. The underlying reason for this could be twofold: (1) Self-regulation is not a unitary construct, and it may have multiple, and perhaps separable, genetic predictors for its subcomponents, or (2) our sample size was not sufficiently large to uncover genetic effects across all self-regulation metrics. Candidate gene studies frequently have several hundred participants in them, and the present study had just 48. There are several published reports of genotype-phenotype associations in relatively small samples. Diamond et al. (2004) found \textit{COMT} rs4680 effects on executive function using a sample of 39 children, and Tsutsumi et al. (2009) found \textit{DRD4} genetic effects on pharmacological effectiveness in just 27 participants. These effects appear to be robust in nature, and large sample sizes are not always required to uncover them.

With any small sample there is always concern over Type I error. We have attempted to reduce our chances of Type I error in a few ways: (1) we only looked for the
main and moderating effects of genes on ERP components with demonstrated associations to self-regulation in our earlier study (see Study 1 in this dissertation); and (2) all statistical tests were calculated robustly. The robust statistical techniques employed here reduce Type I error by utilizing an empirically derived sampling distribution, rather than a theoretically driven one. Thus, observed sample effects are based on an extrapolation of what the distribution would be like in the population.

We are confident that monoamine-related genes, particularly dopaminergic ones, moderate the association between electocortical responses to a selective auditory attention task and real-world self-regulation in typically developing adolescent populations. Extending this work to clinical populations is warranted.
References


cortical structure in attention-deficit/hyperactivity disorder. *Archives of General Psychiatry, 64*(8), 921-931.


4. STUDY 3

Concurrent difficulties in general self-regulatory skills (see e.g., Montague, 2008; Reid, Harris, Graham, & Rock, 2012; Singer & Bashir, 1999), and mental health (e.g., anxiety, depression; Huntington & Bender, 1993; Nelson & Harwood, 2011; Rourke, Young, & Leenaars, 1989) are frequently observed in individuals with a learning disability (LD). Four percent of American children have a comorbid diagnosis of a learning disability and attention-deficit hyperactivity disorder (ADHD; Pastor & Reuben, 2008), and comorbidity rates for the two disorders are estimated to be between 40 and 80% (Tabassam & Grainger, 2002), leading some authors to suggest that learning and self-regulation problems are interrelated disorders which exist on a continuum (Mayes, Calhoun, & Crowell, 2000). Despite the apparent homogeneity in diagnosis, considerable heterogeneity in treatment outcomes occur in these and related disorders (e.g., Mirza, Michael, & Dinan, 1994; Simon & Perlis, 2010).

Literature involving children with attention deficit hyperactivity disorder documents concurrent difficulties in selective attention and poor inhibitory control (Mayes & Calhoun, 2007; Wahlstedt, 2009), and these skills are frequently targeted in therapeutic interventions. Selective attention involves several stages of information processing, i.e., the differentiation of stimulus streams, the selection of the relevant stimulus stream, the suppression of the irrelevant streams, and the maintenance of attention on the relevant information (Määttä, Pääkkonen, Saavalainen, & Partanen, 2005). In the present pilot study, we examined whether selective attention as reflected in event-related potentials (ERPs) during a dual-channel auditory selective attention task can be improved through Integra Mindfulness Martial Arts (MMA) training in a group of children with concurrent learning disabilities and self-regulation challenges (e.g., ADHD).
In such selective auditory attention tasks, ERPs are larger in magnitude for attended, as compared to, unattended tones in typically developing populations. In clinical populations these effects are reduced in size (Stevens, Fanning, Coch, Sanders, & Neville, 2008; Stevens et al., 2013; Stevens, Sanders, & Neville, 2006). In these tasks, participants are asked to pay attention to one auditory stimulus stream while ignoring the other and are required to identify, by pressing a response button, an infrequent “target” stimulus (e.g., high tone) in the specified attended channel. Recording EEG throughout the task allows us to use differences in the amplitude and latencies of ERPs to stimuli in the attended versus unattended ears as indicators of efficient (or inefficient) attentional control. Engagement with the attended stimuli would be reflected in larger neural ERP responses to attended stimuli while disengagement, or suppression, would be reflected in smaller ERP responses to unattended stimuli.

In such dual-channel auditory selective-attention paradigms, target stimuli elicit the ERP components N1, P2, N2, P3 and occasionally an N400/N450. Of particular interest, the N1 reflects the activity of the auditory cortex, with later components reflecting further stages of stimulus processing. Nontarget tones normally elicit only the early occurring N1 and P2 (Hillyard, Hink, Schwent, & Picton, 1973; Nager, Estorf, & Munte, 2006; Woods, 1990), suggesting that attentional resources are quickly withdrawn for the non-response-relevant stimuli. In healthy young adults, the N1 component, as observed over midline fronto-central scalp sites, is typically larger for stimuli in the attended stream (Hillyard et al., 1973; Woods, 1990). Thus, the N1 difference between attended and unattended tones (the N1d effect) is thought to reflect differences in low-level sensory activity (Johnstone, Barry, Anderson, & Coyle, 1996) and this difference in activity is thought to result in the
suppression of an attentional response to unattended tones (i.e., an automatic gating mechanism to reduce further processing of irrelevant stimuli; Singhal, Doerfling, & Fowler, 2002).

In young children ages 3 to 8, a similar but non-identical attention effect has been observed. In a series of studies, Stevens and colleagues (Coch, Sanders, & Neville, 2005; Stevens, Fanning, Coch, Sanders, & Neville, 2008; Stevens, Lauinger, & Neville, 2009; Stevens, Sanders, & Neville, 2006) examined attentional processes in young children. Using a dichotic listening task, different stories were presented to each ear with probes embedded in each story. The children were asked to listen to the story in one ear and ignore the other. In typically developing children, the probes in the attended stream elicited a larger positive going electrocortical response than those in the unattended stream. This difference occurred between 100 and 200 ms post stimulus onset. The authors speculate that this positive going attention effect is not simply a reversal of polarity of the N1 effect in children, but rather it is the absence of an N1 which sometimes occurs due to the complexity and demands of the task (Coch et al., 2005). One other paper has also reported an attention-sensitive positive going waveform in 5-year olds, and although it is presented graphically, it is not otherwise analyzed or discussed (Bartgis, Lilly, & Thomas, 2003, see Figure 2, panel 1).

Our lab group has also replicated such effects, reporting an early frontal positive-going waveform (EFP) correlated with parent reports of their typically developing adolescent's self-regulatory skills (Lackner, Santesso, Dywan, Wade, & Segalowitz, 2013, Study 1 of this dissertation). This work dovetails nicely with the work of Stevens and colleagues. Although they do not take an individual differences approach, Stevens et
al. have reported that selective attention effects are reduced in children from lower SES backgrounds and in children with specific language impairment, a circumstance often associated with poorer attentional control (Stevens, Lauinger, & Neville, 2009; Stevens et al., 2006). In Lackner et al. (2013), we measured self-regulation directly using the Behavior Rating Inventory of Executive Function (BRIEF), a questionnaire measure with demonstrated clinical utility in identifying self-regulation difficulties. Our experience with this measure shows that it is also a reliable individual difference measure. A logical extension of this line of work is to study these same auditory ERPs in special populations where self-regulation is impaired.

Another approach is to consider that these effects can be somewhat normalized through intervention. Two different intervention programs, Fast ForWords (Scientific Learning Corporation, 2007) and the Early Reading Intervention (Kame’enui & Simmons, 2003) have been shown to improve both children's language skills and neural markers of selective auditory attention (Stevens et al., 2008; Stevens et al., 2013). Here, we examine whether training in MMA improves these neural markers of attentional control and/or parent reports of their adolescent's self-regulatory ability. MMA was developed by Paul Badali and Integra, the only accredited children’s mental health centre in Canada dedicated to treating children and youth with learning disabilities and co-occurring mental health issues. MMA integrates mindfulness meditation, cognitive behavior therapy, and behavior modification into a 20-week martial arts group training program. Mindfulness meditation interventions have been used in the past to treat ADHD (van de Weijer-Bergsma, Formsma, Bruin, & Bögels, 2012), but to our knowledge this is
the first program that has been evaluated for youth with LDs and self-regulation challenges.

Clinical interventions for ADHD and LDs vary widely in their intensity. For instance, the Fast ForWord intervention involves 30 consecutive daily training sessions lasting two hours each (Stevens et al., 2008). The Early Reading Intervention involves 40 consecutive daily sessions lasting 30 minutes each (Stevens et al., 2013), and van de Weijer-Bergsma and colleagues (2012) mindfulness meditation intervention involves eight weekly 1.5 hour sessions. A logical question concerns when in the course of treatment that potential ERP and behavioural changes are observed. It could be that 20 weeks are not necessary (or not for all participants) to see evidence for clinical and/or electrophysiological change, and therefore we analyze data at a number of intervals during and following completion of MMA.

We look for evidence of ERP change at both the group level and an exploratory single-subject level using modern robust statistical techniques (e.g., bootstrap resampling, see Wilcox, 2005). Given the frequent heterogeneity of clinical samples, such single subject techniques afford greater statistical power as we can treat each participant as their own case study, examining change in the magnitude of condition effects over time in a single subject. This contrasts with taking a single-subject approach to examining behavioural change as the number of behavioural observations is usually insufficient for bootstrap resampling.

Our approach has two steps: first we examine change in the EFP and N1 components with demonstrated associations in Study 1. In step two we investigate change in all frontal ERP components observed during selective auditory attention tasks (i.e., to
include as well the P2, N2, P3 and N400/N450). Hillyard et al. (1973) have reported that both the frontal P2 and P3 (in addition to the traditionally observed N1) are sensitive to attentional demands in such tasks. Correlative evidence also provides a rationale for investigating these later components. For instance, adults high in impulsivity show reduced frontal P3 amplitudes during a visual task relative to those low in impulsiveness (Carlson, Thai, & McLarnon, 2009). While the centro-parietal N400 is most frequently utilized to study linguistic processing (Kutas & Federmeier, 2011), the frontal N450 component has been documented in non-linguistic auditory contexts (e.g., to tones) in school-aged children (Ceponiene, Rinne, & Naatanen, 2002). Frontally recorded linguistic N400s are sensitive to attention-related manipulations (McCarthy & Nobre, 1993), and for at least some of our participants non-linguistic N400s/N450s may be sensitive to attentional manipulations and sensitive to the effects of training in MMA.

Studies 1 and 2 of this dissertation highlighted the importance of the EFP and N1 in normative non-clinical populations, but this does not preclude the possibility of change in other ERP components. Clinical change can be variable across individuals (see e.g., Brent et al., 1998; Curry et al., 2006; Mirza et al., 1994; Simon & Perlis, 2010), and the current single-subject methods are sensitive to this possibility. The key importance is to have a control group to capture a base rate of effects in this second step. The comparison of treatment and control group results in a test of a single metric – whether the individual shows a change over time.
The goals of the present investigation were threefold:

1) To examine the existence of the Lackner et al. (2013) EFP effect in a similarly aged clinical population, and to see if treatment focused on increasing self-regulation increases the EFP effect.

2) To see if MMA treatment leads to change in selective auditory attention ERP effects not explainable by age-related change using group and single-subject analyses.

3) To see if MMA treatment leads to change in self-regulation as indexed by parent-report BRIEF scores at the group level.

Methods

Participants

Nineteen young male adolescents between the ages of 13 and 16 (16 with an LD and ADHD, 3 with an LD and subclinical ADHD scores as measured by the Conners’ Rating Scale, Multi-Health Systems Inc.) were either caregiver or parent referred to Integra. All participants met Integra’s intake criteria, which includes having a psychoeducational assessment that indicates average or above levels of cognitive ability with levels of academic achievement that are significantly lower than predicted based on the level of cognitive ability. Adolescents also had to be struggling with social, emotional and/or behavioural problems. Twelve of the participants were enrolled in MMA, and seven were on a wait-list for Integra programming and had expressed an interest in participating in MMA.
Measures and Procedures

In order to determine whether the treatment program induced electrophysiological change, each adolescent was given a selective auditory attention task while having their electrophysiological responses recorded, three or four times, at approximately 6 to 8 week intervals. Parents were asked to complete the BRIEF at each session. Testing sessions occurred in a lab at the Psychology department of Ryerson University, one before MMA training began, one midway during training, one after training, and one follow-up three months after training had completed.

Some participants were unable to attend all four testing sessions. Moreover, only certain participants attended the fourth electrophysiological testing session. Perhaps owing to the large time investment required, 5 participants opted not to attend the final testing session (2 in the treatment and 3 in the control group). In an attempt to create a more homogeneous sample for EEG analyses, 5 participants did not have EEG measured at session four (4 treatment and 1 control). Only those with a comorbid diagnosis of an LD plus ADHD provided EEG data (n = 11 at session four). The others either chose not to attend, or only provided electrocardiographic and questionnaire data. In order to maximize power, data for all available sessions is analyzed here. Removing participants who did not attend all four EEG sessions would reduce the sample size dramatically and make some of the analyses severely underpowered. At session one the final sample with electrophysiological data was 16, session two 17, session three 18, and session four 11. Only 8 participants completed all four EEG assessments. At session one the final sample with questionnaire data was 19, session two 18, session three 19, and session four 16. Fifteen participants had complete BRIEF data across all four sessions.
Integra Mindfulness Martial Arts (MMA; Badali & Integra, 2002). MMA is a 20-week manualized group treatment for adolescents with LD and mental health challenges. It is transdiagnostic in its approach, treating adolescents with a broad range of mental health disorders (e.g., ADHD, anxiety, depression, oppositional defiant disorder) and LD profiles together to improve emotion regulation and mental health. Thus, its focus is on improving self-regulation skills that are a deficiency common to all the diagnostic criteria. MMA combines elements of mindfulness, cognitive therapy, and behavioural activation and embeds these therapeutic components into a mixed martial arts and yoga training program. This milieu is designed to enhance youth engagement and to provide in-session physical challenges to allow youth a safe and supportive place to practice therapeutic strategies. Groups include 8 youth and 1-2 graduate-level trained instructors with expertise in mindfulness and martial arts. Each weekly group session is 90 minutes in length, with a check in with youth, parents and the instructor at the end of each session to promote home practice and generalization of skills. Home practice is encouraged and monitored.

Selective auditory attention task. Participants were seated in an electrically shielded room. Two digitized sounds were presented using Etymotic ear inserts (Etymotic Research Inc.). These stimuli consisted of a 1000 Hz (88% probability, nontarget) and a 2000 Hz (12% probability, target) 200 ms tones. During an initial practice block, participants were presented with an example of each type of stimulus and asked to perform 10 practice trials whereby sounds were presented with a variable interstimulus interval of 600 to 800 ms randomized across ears. Participants were instructed to attend to one ear only and to ignore all sounds presented to the other ear. While remaining
visually fixated on a cross at the centre of the computer screen, they were asked to respond by pressing a number on a key pad when they heard the target tone in the attended ear, and not to respond otherwise. Task instructions were presented in written form on the computer monitor while concurrently read aloud by a pre-recorded female voice. The test trials included four blocks of 200 trials each. Trial breakdown across the entire task was as follows: forty-eight 2000 Hz tones presented to the attended ear (attended targets), forty-eight 2000 Hz tones presented to the unattended ear (unattended targets), three-hundred and fifty-two 1000 Hz tones presented to the attended ear (attended non-targets), and three-hundred and fifty-two 1000 Hz tones presented to the unattended ear (unattended non-targets). After the completion of each 200-trial block, there was a 20-second break and participants were then asked to switch their ear of attention and to respond to target tones in that ear only. All participants began the task attending to their right ear. The task took approximately 15 minutes to complete.

**EEG recording and data preprocessing.** EEG was recorded at 64 scalp sites (BioSemi) at a sampling rate of 512 Hz with 0.1-100 Hz analog filtering. Data were re-referenced offline to the average of all sites, then subjected to an independent components analysis. Data were first pruned to exclude any periods of off-task time (e.g., breaks), any excessively noisy channels, and any linked channels and were then subjected to an extended infomax independent components analysis (ICA; Bell & Sejnowski, 1995; Makeig, Debener, Onton, & Delorme, 2004). Data were referenced offline to the average of all sites, filtered (1-30 Hz) and all independent components representing eye movements, heart rate, or other muscle activity were removed. All channels were then
interpolated to a standard scalp montage by spherical spline. See Desjardins and Segalowitz (2013) for further preprocessing details.

The data were then projected back to the scalp and averaged into ERP segments of 1000 ms for target and standard tones correctly responded to in the attended and unattended ears separately, including a 200 ms prestimulus baseline. Peak amplitudes and latencies were clearly maximal over midline sites, as is traditionally found for the N1. Analyses involving ERP amplitudes included an average of 6 frontal channels where the early ERPs were maximal (F1, F2, FC2, FC1, Fz, FCz). Averaging the electrical activity of several sites together allows for individual differences in brain morphology to be less of a concern, and is a strategy commonly used in studies of development.

**Behavior Rating Inventory of Executive Function (BRIEF; Psychological Assessment Resources, Inc)**. The BRIEF parent report form is an 86-item measure that asks parents to evaluate their child’s daily behavior with respect to eight domains of self-regulation. The overall *Global Executive Composite* (GEC) is divided into eight theoretically and empirically derived scales which are then combined to form two indices, the *Behavior Regulation Index* (BRI) and the *Metacognition Index* (MI). The BRI (subscales: Inhibit, Shift, and Emotional Control) represents the child’s ability to utilize appropriate inhibitory control in the service of shifting cognitive set, modulating emotions, and modulating behavior. The MI (subscales: Initiate, Plan/Organize, Working Memory, Organization of Materials, and Monitor) represents the child’s proficiency at self-managing tasks and self-monitoring. T scores were used such that higher scores represented greater difficulty with regulatory skill.
Data Analysis

**Electrophysiology.** ERP data were analyzed using bootstrap resampling techniques at both the group and single-subject level. These techniques are useful when there are no expectations of normality (such as with ERPs), for quantifying effects across the entire time-course of ERPs, and when sample sizes are necessarily small (e.g., Desjardins & Segalowitz, 2013; Rousselet & Pernet, 2011). In addition to the case-study motivation for the present study, this technique is not applicable to data from Studies 1 and 2 because those data were collected on an earlier EEG system with salt-water based electrolyte which often provides inadequate stationarity of the signal to yield stable single-trial segments.

The bootstrap technique is superior to traditional parametric tests (e.g., t-tests and F-tests) as it is an assumption-free statistical test (e.g., there is no need to make unverifiable and/or invalid assumptions about probability distributions prior to analysis; Di Nocera & Ferlazzo, 2000). An empirical sampling distribution of differences is built rather than a theoretically assumed one in order to test for statistical significance. Bootstrap techniques yield increased power, provide greater control over Type I error, and result in more accurate confidence intervals than parametric tests, and are therefore described as being robust (Wilcox, 2005).

In addition to the group level analysis, each participant's electrophysiological data was analyzed for condition differences at each session using a single subject percentile bootstrap test (Wilcox, 2005). Similar bootstrap techniques have shown promise for studying single-subject N170s, error-related negativities, feedback-related negativities and P3s (Lackner et al., 2014; Oruc et al., 2011; Rousselet, Gaspar, Wieczorek & Pernet,
Rousselet and Pernet (2011) call for all ERP researchers to move towards an analysis of all data points using single-trial information, and tout the benefits of single-subject modelling. Here, I address their call for action by looking for attended-minus-unattended condition differences to target tones at the group and single-subject level using single trial data.

Using a custom in-house script in Matlab™, for each ERP data point we sampled with replacement trials from the participant's original data and calculated the 20% trimmed mean. This was repeated 1000 times yielding 1000 estimates of a participant's ERP for a given condition (a bootstrap sample). A second bootstrap sample was calculated for the other condition of interest in the focal comparison. Differences between these two condition's bootstrap samples were then calculated. These difference scores were sorted in ascending order and the upper and lower bounds of the middle 95% of these differences formed the confidence interval. When the confidence interval of the difference does not include zero, then a statistically significant difference between conditions exists for that data point. Condition effects needed to persist for more than 6 ms to be considered a valid effect. This is a conservative approach which allows for further control over Type I error.

In order to address goal #1 of the present study (focusing on the EFP), we examined both the group level and single-subject bootstrap statistics for ERP evidence of AT UT stimulus differentiation as a function of treatment.

In the exploratory single-subject analyses to examine electrophysiological change across sessions (goal #2 of the present investigation) we identified each participant's ERP components (i.e., we identified the EFP, N1, P2, N2, P3 and N4 for each person) and to
see whether significant condition differences exist during the timing of that component.

We then looked for evidence of new ERP effects across sessions, always using their first session as a baseline comparison. For instance, if participant 1 at session two showed an appropriately directed EFP effect (that is, AT more amplified than UT, for instance) but this same participant had not shown an EFP effect at session one, the session two effect would be labelled as a new effect. This allows us to control for pre-existing ERP effects (e.g., a participant may have shown a normative N1 effect at session one). Change in ERPs may happen relatively quickly for some participants (e.g., at session two) but for others it may take more time for these ERP effects to reveal themselves (e.g., not until sessions three or four), and our method is sensitive to these possibilities.

**Behaviour.** In order to examine change over time in participant's BRIEF scores (both the BRI and MI subscales, goal #3 of the present investigation), we ran robust bootstrap t-tests. Our bootstrapped-based approach reduces concern over underpowered analyses.

We tested for significant change in BRIEF scores between session one and the other sessions, separately for the control and treatment groups. This approach allows us to examine dosage-related effects in MMA treatment outcomes. We did not compare all possible permutations of session scores in order to reduce the likelihood of Type I error and to simplify the interpretation of observed effects. An alternative approach may have been to perform a 2(group) x 4(session) mixed-model ANOVA on BRIEF scores, but given the relatively small sample size, and large amount of missing data such an analysis would have been underpowered.

To examine behavioural change at the group level, we employed Wilcox's rm2miss and yuenbt functions in R (an open-source statistics program), for dependent and
independent group level comparisons, respectively (Wilcox, 2005). Both of these functions are based on a bootstrapped t-method, and their underlying computations have been extensively documented elsewhere.

Results

Change in the EFP Effect over Time

Grand averaged ERP data for all conditions, sessions and groups can be seen in Figure 3.1. An EFP with the expected latency and morphology was elicited at nearly all sessions and for all groups. However, AT-UT stimulus differentiation was not apparent during this time window. An examination of Figures 3.2 and 3.3 shows that zero of seven control participants and three of twelve participants in the treatment group showed evidence for ‘optimization’ of the EFP effect over time (i.e., amplified EFPs for attended rather than unattended stimuli). Entering these proportions into a chi-squared analysis showed that the groups did not differ in EFP optimization, $\chi^2(1) = 2.078$, $p = .15$.

Electrophysiological Change over Time

As can be seen in Figure 3.1, across all sessions and groups, stimulus conditions were not differentiated at the timing of any ERP component of interest. However, the lack of a group level effect does not preclude the existence of single-subject effects which now follow.

Results of the single subject bootstrapping procedure can be seen in Figure 3.2 for the control group and Figure 3.3 for the treatment group. Where no data are presented for a participant, this indicates that either they did not attend that testing session, or their data were unusable (e.g., too much noise, failure to follow task instructions etc).

Two of seven participants in the control group showed a new ERP effect in the optimal direction not observed at their first testing session (see Figure 3.2). The first of
these two participants showed evidence of change to the P3, while the second participant showed change to the N1. Thus, the passage of time alone yielded changes to ERPs in two of seven cases.
Figure 3.1: Grand averaged waveforms for attended and unattended target tones for each participant group and each session. The second panel on each overlay depicts the confidence interval around the condition differences for the contrast of interest.
Nine of twelve participants in the treatment group showed an ERP effect of the 'optimal' direction (i.e., amplified ERPs for attended rather than unattended stimuli) that had not been observed in their first testing session. Three showed an optimization of the EFP effect, 2 an optimization of the N1 effect, 1 an optimization of the P2, 3 an optimization of the N2 effect, 2 an optimization of the P3 effect and 2 an optimization of the N4 effect.

When these proportions were entered into a chi-squared analysis (2/7 versus 9/12 participants showing change), significant group differences were uncovered, $\chi^2(1) = 3.909, p = .04$. More participants in the treatment group showed evidence for electrophysiological change across sessions than did participants in the waitlist control group.

Additionally, we looked to see in how many participants non-optimal effects emerged over time, (i.e., amplified ERPs for unattended rather than attended stimuli) that had not been observed in their first testing session. In the treatment group 4 of 12 participants showed a new effect in the non-optimal direction, and in the control group 3 of 7 participants showed a new non-optimal effect. Entering these proportions into a chi-squared analysis showed that these proportions did not differ from one another, $\chi^2(1) = .172, p = .68$.

Another, albeit more conservative way of analyzing the data would be to consider the number of total ERP components that could potentially show evidence of change or optimization over time (i.e., the number of ERPs compared to one another). In the treatment group there were 156 ERP components examined for change (4 participants had all 4 session's data with 6 ERP components compared 3 times, and therefore 18 ERPs
were compared, 6 more had 3 sessions of data and therefore 12 ERP component comparisons, and 2 participants had 2 sessions worth of data and therefore 6 ERP components with a chance to change; (4 x 18) + (6 x 12) + (2 x 6) = 156). In the waitlist group there were 102 possible components which could show change (4 participants had all 4 session's data and therefore 18 ERP components with a chance to change, 2 more had 3 sessions of data and therefore 12 ERP components to change, and 1 had 2 sessions worth of data and therefore 6 ERP components with a chance to change; (4 x 18) + (2 x 12) + (1 x 6) = 102). In the treatment group there were 16 optimal-direction ERP effects (13 new ERP effects, plus the three that were maintained to a subsequent testing session), and in the control group there were 4 optimal-direction ERP effects. Entering these proportions into a chi-squared analysis (16/156 and 4/102) yielded a non-significant result, with a trend in the expected direction, $\chi^2(1) = 3.46, p = .06$. A similar analysis using non-optimal direction effects yielded no significant differences between the groups $\chi^2(1) = .15, p = .70$.

Some of the optimal ERP effects were maintained over time, and some were not. In the treatment group, 2 of the 9 participants with new ERP effects (22%) maintained them to a following testing session. Many of the new effects appeared at the participant's final testing session and may have continued on into the future, but electrophysiological data are not available to support this claim. It is likely that more than 22% of them were maintained over time. In the control group 0 of 4 new ERP effects were maintained to a following session, with only one of these effects appearing in the participant's final testing session. Comparing the number of ERP effects maintained across sessions between the two groups in a chi-squared analysis did not reveal significant group
differences in maintenance, $\chi^2(1) = 2.21, p = .29$, but as previously stated this analysis likely underestimates the potential for these new ERP effects to carry forward. If we examine evidence of maintenance of change not including the last session, then 3 of the 6 changes (involving 2 individuals) were maintained in the treatment group and none in the control group.
Figure 3.2. Results of the single subject bootstrapping procedure for the condition comparison at each testing session for the waitlist control group. ERPs to attended targets are shown in red, and ERPs to unattended targets are shown in blue. The bottom panel of each figure shows the $p$ value associated with each contrast. When the grey line dips below the black dotted line ($p = .05$) a significant difference between conditions exists.
Figure 3.3. Results of the single subject bootstrapping procedure for the condition comparison at each testing session for the treatment group. ERPs to attended targets are shown in red, and ERPs to unattended targets are shown in blue, with the confidence intervals about the difference in dashed grey lines. The bottom panel of each figure shows the p value associated with each contrast. When the grey line dips below the black dotted line ($p = .05$) a significant difference between conditions exists.
Behavioural Change over Time

We looked for change in BRIEF scores across pairs of sessions using Wilcox’s (Wilcox et al., 2014) robust group level comparison procedures\(^5\). We first discuss the session one equivalency of the two groups, and then discuss change in the treatment group followed by change in the control group. Looking for evidence of change in the waitlist control group allows me to rule out age- and retest-related change as an explanation for treatment effects. For these analyses I only used participants with complete questionnaire data for both sessions of interest.

**Session one group comparisons.** At session one, the groups did not differ overall on their MI or BRI scores. See Table 3.1.

<table>
<thead>
<tr>
<th>scale</th>
<th>Treatment group session one estimate</th>
<th>Control group session one estimate</th>
<th>Estimate of score differences</th>
<th>Lower confidence interval around the difference</th>
<th>Upper confidence interval around the difference</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>350.00</td>
<td>325.29</td>
<td>24.71</td>
<td>-9.24</td>
<td>58.67</td>
<td>.13</td>
</tr>
<tr>
<td>BRI</td>
<td>192.5</td>
<td>180.43</td>
<td>12.07</td>
<td>-18.24</td>
<td>42.38</td>
<td>.39</td>
</tr>
</tbody>
</table>

Note: There are 8 participants in the control group here rather than the 7 depicted with ERP data in Figure 3.2. as one control participant did not produce useable ERP data, but was included in these behavioural analyses.

**Control group. Change in Metacognition Index.** The control group showed no change in their MI scores over time. Comparisons are summarized in Table 3.2.

---

\(^5\) Given the small number of participants with complete data at session four, the most powerful comparison involves the contrast of sessions one and three. The comparison between session one and session four should be considered exploratory in nature, and should be interpreted with caution.
Table 3.2: Control Group Change in MI Scores across Sessions

<table>
<thead>
<tr>
<th>Session comparison</th>
<th>Session 1 estimate of MI scores</th>
<th>Session 2, 3 or 4 estimate of MI scores</th>
<th>Estimate of MI score differences</th>
<th>Lower confidence interval around the difference</th>
<th>Upper confidence interval around the difference</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessions one and two</td>
<td>331.64</td>
<td>334.56</td>
<td>-2.92</td>
<td>-23.63</td>
<td>2.12</td>
<td>.09</td>
</tr>
<tr>
<td>Sessions one and three</td>
<td>324.0</td>
<td>320.75</td>
<td>3.25</td>
<td>-39.50</td>
<td>55.62</td>
<td>.61</td>
</tr>
<tr>
<td>Sessions one and four</td>
<td>327.12</td>
<td>313.9</td>
<td>13.22</td>
<td>-10.89</td>
<td>37.89</td>
<td>.24</td>
</tr>
</tbody>
</table>

Control group. Change in Behaviour Regulation Index. The control group's BRI scores also did not change over time. See Table 3.3.

Table 3.3: Control Group Change in BRI Scores across sessions

<table>
<thead>
<tr>
<th>Session comparison</th>
<th>Session 1 estimate of BRI scores</th>
<th>Session 2, 3, or 4 estimate of BRI scores</th>
<th>Estimate of BRI score differences</th>
<th>Lower confidence interval around the difference</th>
<th>Upper confidence interval around the difference</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessions one and two</td>
<td>190.08</td>
<td>179.16</td>
<td>10.92</td>
<td>-16.42</td>
<td>12.20</td>
<td>.82</td>
</tr>
<tr>
<td>Sessions one and three</td>
<td>194.0</td>
<td>190.75</td>
<td>3.25</td>
<td>-49.87</td>
<td>27.48</td>
<td>.49</td>
</tr>
<tr>
<td>Sessions one and four</td>
<td>183.77</td>
<td>159.14</td>
<td>24.64</td>
<td>-8.77</td>
<td>57.10</td>
<td>.14</td>
</tr>
</tbody>
</table>

Treatment group. Change in Metacognition Index. The treatment group demonstrated an improvement in their MI scores from sessions one to two and one to three. No change was observed from sessions one to four, but this is perhaps owing to the small sample size at session four. See Table 3.4.
Table 3.4: Treatment Group Change in MI Scores across Sessions

<table>
<thead>
<tr>
<th>Session comparison</th>
<th>Session 1 estimate of MI scores</th>
<th>Session 2, 3 or 4 estimate of MI scores</th>
<th>Estimate of MI score differences</th>
<th>Lower confidence interval around the difference</th>
<th>Upper confidence interval around the difference</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessions one and two</td>
<td>341.07</td>
<td>325.0</td>
<td>16.07</td>
<td>11.45</td>
<td>32.24</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sessions one and three</td>
<td>345.18</td>
<td>324.44</td>
<td>20.74</td>
<td>1.28</td>
<td>35.89</td>
<td>.038</td>
</tr>
<tr>
<td>Sessions one and four</td>
<td>347.0</td>
<td>329.28</td>
<td>17.72</td>
<td>-20.23</td>
<td>42.71</td>
<td>.43</td>
</tr>
</tbody>
</table>

**Treatment group. Change in Behaviour Regulation Index.** We followed the same procedure as above to look for change in BRI scores across sessions. At the group level, there was no improvement in BRI scores for any of the session comparisons. See Table 3.5.

Table 3.5: Treatment Group Change in BRI Scores across sessions

<table>
<thead>
<tr>
<th>Session comparison</th>
<th>Session 1 estimate of BRI scores</th>
<th>Session 2, 3, or 4 estimate of BRI scores</th>
<th>Estimate of BRI score differences</th>
<th>Lower confidence interval around the difference</th>
<th>Upper confidence interval around the difference</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessions one and two</td>
<td>187.08</td>
<td>190.41</td>
<td>-3.32</td>
<td>-10.01</td>
<td>15.42</td>
<td>.70</td>
</tr>
<tr>
<td>Sessions one and three</td>
<td>189.93</td>
<td>185.92</td>
<td>4.02</td>
<td>-7.03</td>
<td>15.69</td>
<td>.43</td>
</tr>
<tr>
<td>Sessions one and four</td>
<td>187.08</td>
<td>191.97</td>
<td>-4.89</td>
<td>-17.15</td>
<td>20.77</td>
<td>.84</td>
</tr>
</tbody>
</table>

**Range of Self-Regulatory Difficulties**

In Lackner et al. (2013) we found that only good but not poor self-regulators differentiated AT and UT stimuli during the EFP, and here we found very few participants with any EFP differentiation. We conducted an exploratory analysis to see
why this may be the case, and hypothesized that it may be due to the range of self-regulatory abilities in each sample. All of our participants in Study 1 of this dissertation had BRIEF scores in the top 47% of the T-score distribution (range 1-47%), and only the best of those participants showed EFP condition differences. However, our current MMA participants and waitlist control group had BRIEF T-scores below this range (47-87%). Thus, the distributions are non-overlapping. Because our participants did not show an EFP in the hypothesized direction, and because of the increased self-regulatory difficulties observed in the present sample, we did not look for associations between self-regulatory skill and specific ERP components.

Discussion

In this study we examined ERPs elicited by a selective auditory attention task that have been found to relate to individual differences in self-regulation in healthy adolescents (Lackner et al., 2013) in a clinical sample taking part in an intensive treatment designed to improve self-regulation skills. If the frontally based EFP waveform differentiation reported in Study 1 (Lackner et al., 2013) is related to self-regulatory ability, then manipulating this skill may alter the ERP. Our first examination was of the EFP given this was the individual differences effect found earlier. A further exploratory analysis examined the entire ERP waveform in single-subject analyses, comparing the treatment group and control group. Thus, the goals of the present investigation were threefold: (1) To look for an effect of an ERP component similar to the EFP from Lackner et al. (2013) in a clinical population and to see if MMA leads to an EFP effect; (2) To see if MMA leads to change in selective auditory attention ERP effects not explainable by age-related change; and (3) To see if MMA leads to change in self-
regulation as indexed by parent-report BRIEF scores. Here I address each of these goals in turn. Where possible, these goals were addressed at both the single-subject and group levels.

**Effects of Treatment on Selective Auditory Attention ERP Effects**

When ERPs were averaged across participants in both the treatment and control groups there was no evidence for change over time. In fact, neither group differentiated AT and UT stimuli during any specific ERP component or any testing session. This is perhaps owing to the nature of this population. Lackner et al. (2013; Study 1 of this dissertation) found stimulus differentiation only in good self-regulators, which were lacking in the present study. Even after treatment the current participants still had BRIEF scores in the clinically significant range, and therefore we may not expect condition differences at least in the early ERP components in this population. The later ERP components (e.g., P3 and N4) have not been previously examined using this task and this population. Therefore, we had no a priori predictions about these later ERP components. At the group level it appears that the present sample is also unable to discriminate stimulus conditions during this latency in this small sample.

In our study, the distributions of BRIEF scores were non-overlapping with those in Study 1, where only the good-self regulators showed a significant EFP condition difference. We might expect to see AT-UT EFP differentiation in our clinical sample if the treatment were able to increase their self-regulatory skill to the level of our best self-regulators in Study 1; this would likely require very intensive intervention and did not happen in the 20-week program.
Robust single subject statistics allowed us to examine electrophysiological change within individuals across a number of testing sessions. This is akin to a clinical case-study approach, and is an important approach to take given the heterogeneous outcomes that can occur as a result of therapeutic intervention (e.g., Mirza et al., 1994; Simon et al., 2010). Single subject statistics were aggregated at the group level to examine whether more young adolescents enrolled in the MMA program showed optimal change over time in their various ERP markers of selective auditory attention than young adolescents who were on a wait-list for this same program. In auditory selective attention tasks, the pattern of ERPs associated with the most favourable outcomes is that where ERPs are amplified to task relevant stimuli and suppressed or reduced to to-be-ignored stimuli. Positive-going waveforms such as the P2 should be more positive for attended, rather than unattended, stimuli, while negative going waveforms such as the N1 should be more negative for attended rather than unattended stimuli. While each ERP component may have different psychological correlates, such an overall pattern of ERP differentiation suggests that greater attention allocation is placed on the task relevant stimuli, and that a greater depth or consistency of processing subsequently occurs to those stimuli.

We found that this pattern of optimal change emerged more over time in the treatment group than in the control group while there was no group difference in change reflecting non-optimal stimulus differentiation.

Thus, participating in an intervention designed to improve self-regulatory skill (MMA) did not always lead to treatment group changes in the EFP, the early frontal component with documented correlations to self-regulatory skill (Lackner et al., 2013). Just three of twelve treatment participants showed an 'optimization' of the EFP effect in
response to the MMA program. Others began to show appropriately directed effects during other slightly later ERP components including the N100, P200, N200, P300 and N400/N450. Significantly more individuals in the treatment group showed such effects than in the waitlist control group. As with all treatment studies, the important comparison is with the control group as we may expect to find natural growth or retest effects over time. The results of this intensive but small scale study are suggestive and need to be followed up. The exploratory analysis may potentially lead us to consider further useful studies.

Our data did show that the effects of MMA on electrophysiology are variable across individuals. Given that ERP components are associated with partially dissociable cognitive operations, examining which ERP components showed change over sessions within particular individuals may give us clues to how the treatment was internalized by that individual, and may help us develop more targeted hypotheses for that individual's continued change.

Speculation on how each ERP component may be influenced by the intensive MMA intervention depends on the functional relations of the component. The N1 difference between attended and unattended tones (the N1d effect) is thought to reflect differences in low-level sensory activity (Johnstone et al., 1996) and this difference in activity is thought to result in the suppression of an attentional response to unattended tones (i.e., an automatic gating mechanism to reduce further processing of irrelevant stimuli; Singhal, Doerfling, & Fowler, 2002). Other early processes involved in the task include the formation of a percept of the stimuli, and attention to task-relevant features. Therefore we can speculate that participants who show electrophysiological evidence for
change at very early stimulus processing stages may benefit from MMA at an implicit level that affects their bottom-up processing. They may have learned to automatically filter out irrelevant information. However, this is only speculation at this point and requires further study.

Similarly, we may speculate that increases in frontal P3 amplitude may reflect improvement in perceptual discrimination skills (Wronka, Kaiser, & Coenen, 2008), and for at least some of our participants improvement in N400/N450s differentiation as evidence for sensitivity to attention manipulations.

**Effects of Treatment on Parent-Report Self-Regulation**

Previous studies of the effectiveness of the MMA program have largely failed to detect significant change in self-regulation pre- versus post-intervention as indexed by BRIEF scores (unpublished research by Badali and Milligan). One exception to this general pattern is a subgroup of children diagnosed as having the hyperactive/impulsive subtype of ADHD who showed improvements to their ability to monitor their own behaviour (as indexed by the Monitor subscale of the BRIEF, part of the Metacognition Index; Haydicky, Wiener, Badali, Milligan, & Ducharme, 2012), but overall evidence for significant change in BRIEF scores was minimal. This was true of the present sample when examining change to BRI scores across all sessions and MI scores from session one to session four. However, we did find some evidence for change in MI scores from session one to sessions two and three. Therefore, while further work with larger sample sizes is required to fully evaluate the effectiveness of the MMA program, we cannot discount the likelihood that it can lead to true behavioural change. Qualitative research on
the MMA program has suggested improvements to both parent- and self-report self-regulatory skill (Milligan, Badali, & Spiroiu, 2013), and our findings are in line with this. Using robust statistics, we were able to detect significant improvements in some facets of self-regulation in some individuals who underwent MMA training, and observed little behavioural improvement in individuals who were on a waitlist for the same intervention.

All MMA participants showed a rapidly significant reduction in problematic MI behaviour. MI scores represent the child’s proficiency at self-managing tasks and self-monitoring. MI T-scores decreased significantly from session one to session two, just 6 weeks later. However, previous studies documenting electrophysiological change as a function of treatment typically use a highly intensive treatment program. For instance, increased differentiation of early ERP amplitudes related to selective auditory attention have been demonstrated after intervention with the FastForWords program, which requires 30 days of 2 hour treatment sessions (Stevens et al., 2008). The Early Reading Intervention has also led to improvements in ERP indices of selective-auditory attention, but requires a 30-minute intervention 5 days per week, for 8 weeks in a small group in order to show such change (Stevens et al., 2013). In contrast, the MMA intervention only requires a weekly 90-minute intervention, and although the intervention lasts for 20 weeks, weekly practice in MMA may not be intense enough to elicit change in those with the poorest self-regulatory skills.

The MMA intervention did not lead to significant change in BRI scores. BRI scores represent the child’s ability to utilize appropriate inhibitory control in the service of shifting cognitive set, modulating emotions, and modulating behavior. The present
pattern of results indicating the MI, rather than the BRI, is most sensitive to change as a function of intervention is consistent with the work of Lackner et al. (2013). Individual differences in MI scores correlated with ERPs indexing a suppression of information processing to to-be-ignored stimuli (Lackner et al., 2013). To the extent that MMA also trains participants to filter out irrelevant information, we would also expect to see change in this correlated behavioural measure.

One unknown when starting this study was what the effect would be of having participants selected specifically because they have low scores on self-regulation. Conceivably this may make improvement highly likely given the large room for increased self-regulation. Alternatively, it may be the case that very low levels of self-regulation as reflected in behaviours described in the BRIEF scales would result in little movement due to well entrenched maladaptive habits. It is also the case that the MMA program, being one that emphasizes intense focusing of attention, may affect the ERP more than real-world BRIEF behaviours. This could happen because more focused attention increases ERP amplitude both because of increased recruitment of cortical generators underlying the EEG and because of increased consistency of response of the single trials contributing to the averaged ERP. Behaviours outside the lab testing context are necessarily more complex, and are affected by more factors than attention control.
References


142


Stevens, C., Fanning, J., Coch, D., Sanders, L., & Neville, H. (2008). Neural mechanisms of selective auditory attention are enhanced by computerized training:


Growth in self-regulatory skill continues into late adolescence and emerging adulthood (Boelema et al., 2014; Luciana, Conklin, Hooper, & Yarger, 2005; Steinberg, 2004). Individual differences in self-regulation during late adolescence and emerging adulthood are correlated with individual differences in social and physical health (Hall, Fong, Epp & Elias, 2008; Pronk & Karremans, 2014), and risk-taking (Patrick, Blair, & Maggs, 2008; Pharo, Sim, Graham, Gross, & Hayne, 2011), to name a few consequences. Thus it is important to understand the correlates of self-regulation during these often overlooked years of development, such as frontal brain regions supporting self-regulation that are observed to still be growing at age 20 (Fuster, 2002; Giedd, 2004, 2008).

Self-regulation, a collection of skills required for purposive, goal-directed behaviour, has been conceptualized in somewhat distinct ways by different categories of social science researchers. The neuropsychological tradition (and more recently educational psychology) has tended to refer to this collection of behaviours as executive functions, and cognitive psychologists make reference to cognitive control. Regardless of how self-regulation is labelled, it contains some aspect of selective attention, whether selective attention is considered a prerequisite for self-regulation or a crucial component therein (Fonagy & Target, 2002; MacCoon, Wallace, & Newman, 2004; Rueda, Posner, & Rothbart, 2004; Ruff & Rothbart, 1996). In this study, we focus on real-world self-regulation, that is, self-regulatory skill as it plays out in real-world contexts. Takeuchi et al. (2013) refer to this set of behaviours as Executive Functions during Everyday Events (or EFEEs), underscoring the conceptual overlap between executive functions and self-regulation.
Research has uncovered important electrophysiological predictors of self-regulation, many of which are generated by prefrontal cortex activation. For instance, both children and adults with attention-deficit hyperactivity disorder (ADHD), a condition that involves marked impairments in self-regulation, show aberrations in frontal recruitment while performing a Go-NoGo task (Fallgatter et al., 2005; Fallgatter et al., 2004) and abnormal P300s during a visual discrimination task (Gumenyuk et al., 2005). Thus far, the investigated electrophysiological correlates of self-regulation are relatively restricted to the later stages of information processing. However, Lackner et al. (2013, see Study 1 of this dissertation) reported that reduced amplitudes of a new, early occurring ERP marker recorded during a selective auditory attention task to to-be-ignored sounds predicted individual differences in self-regulation in 12-14 year olds. We termed this event-related potential (ERP) the early frontal positivity (or EFP). We additionally found that reduced N1 latency to targets in the unattended ear predicted self-regulatory skill. However, continued growth to self-regulatory skill as well as electrophysiological change after this time window (see e.g., Giedd, 2004) bring in to question the long term stability of such effects. Our goals were to see if the early frontal positivity uncovered by Lackner et al. (2013, Study 1) and observed again in Study 3 of this dissertation, was also observed in a young adult sample, and to see whether this component had predictive value over self-regulatory skills during this later developmental stage just as it does in early adolescence.

Amplitudes in the averaged ERP can differ across participants because of differences in the amplitude of the electrocortical generators (event-related spectral perturbations – ERSPs), or because of differences in the consistency of EEG phase angle (intertrial coherence – ITC). The trial-to-trial consistency of responding can be viewed as an
electrocortical form of self-regulation and it may account for behavioural self-regulation on a larger scale. It is not clear which of these interpretations applies to the results of Lackner et al. (2013). Unfortunately, the authors were unable to test these hypotheses because a water-based EEG system was used. Better self-regulation may be correlated with more consistent ERP phase angle responses (ITC) or to changes in power response (ERSP) to attention eliciting stimuli. ERSP is a frequency–domain approach in which time-locked changes in the frequency power spectrum of the EEG data are examined, with the assumption that events in the environment perturb the ongoing rhythmic activity that we observe at the scalp (Makeig, Debener, Onton, & Delorme, 2004). ITC is calculated and plotted as a frequency-by-latency image of the strength of phase locking of EEG signals to particular events of interest (Makeig et al., 2004).

Here we focus on ITC and ERSP in the theta and alpha frequency ranges for several reasons. Alpha activation (8-14 Hz) is inversely associated with cognitive engagement, making it a relevant frequency band to investigate in a task of selective attention. Higher levels of alpha activation have been in interpreted in two ways, as the idling of the cortex when engagement is low (Adrian & Matthews, 1934), and alternatively as evidence for active suppression of sensory information when attention is directed inwards (Cooper, Croft, Dominey, Burgess, & Gruzelier, 2003). Thus, reduced amplitudes to to-be-ignored stimuli in Lackner et al. (2013) may be attributable to low cognitive engagement with such stimuli or to active suppression of these stimuli. While the current study will not be able to address this controversy of interpretation, both interpretations are of theoretical

---

6 Data collected from water-based systems are insufficient for calculating ERSP and ITC due to problems with stationarity. Water-based nets dry out over the course of the recording, thereby introducing noise into any analyses which focus on single trials. This makes the algorithm account for the large noise signals first, reducing the likelihood of isolating components reflecting cortical networks.
interest, as uncoupling the effects of ITC and ERSP would add to our understanding of the causes of our prior findings.

Centrally recorded alpha ITC and ERSP increase across childhood (Bishop, Anderson, Reid, & Fox, 2011) as does alpha and theta coherence (Barry et al., 2004). Self-regulation similarly increases during childhood, leading to the possibility that these processes are developmentally associated with one another. Moreover, adults with ADHD show increased levels of absolute alpha power and atypical alpha asymmetry in comparison to controls (Hale et al., 2009; Koehler et al., 2009) and girls with ADHD show an atypical developmental pattern of intrahemispheric coherence (Barry, Clarke, McCarthy, & Selikowitz, 2006). Intriguingly, alpha coherence across sites is associated with individual differences in aspects of emotional self-regulation. Traditional alpha EEG coherence measures correlate with levels of state anxiety (Hinrichs & Machleidt, 1992; Knyazev, Savostyanov, & Levin, 2005; although the direction of the relationship is unclear), and aggressive cognition (Hinrichs & Machleidt, 1992) in adults. Related measures of phase shifting and locking have been associated with these same variables in adolescence (Lackner et al., 2014). Therefore, alpha generally, and coherence more specifically, may be related to self-regulation outside of clinical contexts.

We additionally examined ITC and ERSP in the theta frequency range. Theta activity (3 – 7.5 Hz) increases when engaged in active problem solving, particularly when it is selective and narrowly focused (Schacter, 1977). It has also been implicated in attentional orienting, which is defined as an alertness, arousal or readiness to process information (Başar, Başar-Eroğlu, Karakaş, & Schürmann, 2001), and as a marker of the
realization of the need for cognitive control (Cavanagh & Frank, 2014).\(^7\) Frontal midline theta is thought to be an important correlate of prefrontal cortex (PFC) functioning generally, and anterior cingulate cortex (ACC) functioning specifically (Asada, Fukuda, Tsunoda, Yamaguchi, & Tonoike, 1999; Luu, Tucker, & Makeig, 2004). Using the modelling software sLORETA, Sauseng and colleagues (Sauseng, Hoppe, Klimesch, Gerloff, & Hummel, 2007) have evidence to suggest that ACC theta activity is related to an attentional system responsible for allocating cognitive resources. Importantly for the present study, in children with ADHD, theta power to targets is increased while performing an auditory oddball task (Yordanova, Heinrich, Kolev, & Rothenberger, 2006) while theta ITC during the timing of the ERN and Pe is reduced in adolescents with ADHD relative to their typically developing peers (Groom et al., 2010).

Therefore, we investigated associations between early occurring ERP markers of attentional control (i.e., the EFP and N1 recorded during a selective auditory attention task) and self-regulation in a group of older adolescents and emerging adults. We additionally investigated the spectral characteristics of the observed effects, namely ERSP and ITC in the theta and alpha range. We expected to replicate our earlier findings of an association between self-regulation, EFP amplitudes, and N1 latencies and expected to see decreased alpha and increased theta ERSP to attended targets, compared to

---

\(^7\) Some research has linked increased theta to drowsiness (Laufs et al., 2006) or to the presence of a hypnagogic state (Schacter, 1977), interpretations which are seemingly at odds with the present interpretation of theta as related to attentional control and problem solving. However, associations between theta and cognition may vary as a function of age (Laufs et al., 2006, assessed adults aged 31 ± 3 years), when relative rather than absolute levels of theta are assessed (Laufs et al., 2006), when theta is measured diffusely or locally from fronto-central sites, or when contributions of tonic and phasic theta are considered (Schacter, 1977). It is also possible that theta that is generated in the context of resting EEG is different from theta generated in the context of the stimulus presentation and processing that underlies ERPs.
unattended targets, particularly in those who are good self-regulators. Further, we predicted reduced theta ITC in poor self-regulators.

Method

Participants

This study included 66 participants ages 19 to 23 (28 males) who were selected based on their participation in an earlier longitudinal study about university adjustment. In this longitudinal study, 590 university students were asked to report on their emotional regulation strategies as well as their tendency to procrastinate (among other measures not of interest here). Although both of these metrics are not specifically designed to assess self-regulation, they share some conceptual overlap with the constructs of interest. We selectively invited males and females with high and low levels of cognitive (procrastination) and emotional self-regulation to participate in the present study. This was done to ensure that we sampled from the full range of self-regulatory abilities. Details of these calculations are supplied below.

All participants were not taking any psychoactive medication, and did not have a history of concussion, epilepsy or serious psychiatric disorders. Participants were given a $60 honorarium for their participation.

Materials

Prescreening measures.

_Difficulties with Emotion Regulation Scale (DERS, Gratz & Roemer, 2004)._ Six items from the original Goals and Strategies subscales were selected for use in the present study. Participants were asked to report how often they behave in a certain manner when upset or stressed. Questions included "When I’m upset or stressed, I have difficulty thinking about anything else", and "When I’m upset or stressed, I know that I can find a
way to eventually feel better." Response options were almost never, sometimes, about half the time, most of the time, and almost always. Responses were reverse coded as appropriate so that higher scores represented poorer emotion regulation strategies. See Appendix D.

**Emotion Reactivity Scale (ERS, Nock, Wedig, Holmberg, & Hooley, 2008).** We used an abridged version of the Emotion Reactivity Scale to additionally assess emotional self-regulation. We asked participants 13 questions distributed across the Sensitivity, Intensity, and Persistence subscales. Sample items include "When I am angry/upset, it takes me much longer than most people to calm down" and "When something bad happens, my mood changes very quickly. People tell me I have a very short fuse." Participants were asked to select from the response options ranging from not at all like me (1) to completely like me (4). Higher scores represented poorer emotional self-regulation.

Participants' scores on the DERS and ERS were z-scored and then summed together to form an emotion regulation composite score. These scores were divided into tertials separately for males and females, and those in the top third of each group were designated as having the poorest emotional regulation strategies, and those in the bottom third of the distribution had the strongest emotion regulation abilities. These calculations included all 590 participants who completed the pre-screening.

**Procrastination Scale (Tuckman, 1991).** Participants were asked 12 of the original 16 questions about their tendency to procrastinate when completing tasks. They responded on a 4-point scale from very true (4) to not at all true (1). Items on the scale include “I needlessly delay finishing jobs, even when they’re important,” “I postpone
starting on things I don’t like to do,” and “When I have a deadline, I wait till the last
minute.” Higher scores represented lower levels of procrastination and thus
approximately higher levels of cognitive self-regulation. See Appendix D.

Scores were once again z-scored and males and females in the highest and lowest
tertials were assigned to high and low cognitive self-regulation groups. Successful
recruitment from each of these quadrants occurred as in Table 4.1, yielding the final
sample of 66 participants.

Table 4.1. Distribution of Cognitive and Emotional Self-Regulation Pre-screening Scores.

<table>
<thead>
<tr>
<th>Males</th>
<th>Best emotional self-regulation</th>
<th>Poorest emotional self-regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best cognitive self-regulation</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Poorest cognitive self-regulation</td>
<td>8</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Females</th>
<th>Best emotional self-regulation</th>
<th>Poorest emotional self-regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best cognitive self-regulation</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Poorest cognitive self-regulation</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>

**Focal measures.**

*Behavior Rating Inventory of Executive Function – Adult Version (BRIEF-A; Psychological Assessment Resources, Inc).* The BRIEF-A is a 75-item measure that asks participants to evaluate their daily behavior with respect to nine domains of self-regulation. The overall Global Executive Composite (GEC) is divided into nine theoretically and empirically derived scales which are then combined to form two
indices, the Behavior Regulation Index (BRI) and the Metacognition Index (MI). The BRI (subscales: Inhibit, Shift, Self-Monitor, and Emotional Control) represents the participant’s ability to utilize appropriate inhibitory control in the service of shifting cognitive set, modulating emotions, and modulating behavior. The MI (subscales: Initiate, Plan/Organize, Working Memory, Organization of Materials, and Task Monitor) represents the participant’s proficiency at self-managing tasks and self-monitoring. Scores were inverted so that higher scores represented higher levels of regulatory skill.

Selective auditory attention task. Participants were seated in an electrically shielded room. Two digitized sounds were presented using Etymotic ear inserts (Etymotic Research Inc.). These stimuli consisted of a 1000 Hz (88% probability, nontarget) and a 2000 Hz (12% probability, target) 200 ms tones. During an initial practice block, participants were presented with an example of each type of stimulus and asked to perform 10 practice trials whereby sounds were presented with a variable interstimulus interval of 600 to 800 ms randomized across ears. Participants were instructed to attend to one ear only and to ignore all sounds presented to the other ear. While remaining visually fixated on a cross at the centre of the computer screen, they were asked to respond by pressing a number on a key pad when they heard the target tone in the attended ear, and not to respond otherwise. Task instructions were presented in written form on the computer monitor. See Appendix B for a graphical representation of the task.

The test trials included four blocks of 200 trials each. Trial breakdown across the entire task was as follows: forty-eight 2000 Hz tones presented to the attended ear (attended targets, subsequently referred to as ATs), forty-eight 2000 Hz tones presented to the unattended ear (unattended targets, subsequently referred to as UTs), three-hundred
and fifty-two 1000 Hz tones presented to the attended ear (attended non-targets), and
three-hundred and fifty-two 1000 Hz tones presented to the unattended ear (unattended
non-targets). After the completion of each 200-trial block, there was a 20-second break
and participants were then asked to switch their ear of attention and to respond to target
tones in that ear only. We counterbalanced whether participants started the task
responding to the sounds in their right or left ear.

**Procedures**

Participants were invited to participate via email. Equal numbers of participants
were contacted from each quadrant, but response rates varied, yielding the sampling
distribution described in Table 4.1. The principal researcher was blind to their pre-
screening characteristics until after testing was completed. Participants came in to the lab
for a three-hour session, and completed the selective auditory attention task along with
several other tasks, not described here.

**EEG recording and data analysis.** EEG was recorded with a gel electrolyte at 128
scalp sites (BioSemi ActiveTwo) at a sampling rate of 512 Hz. Seven additional
electrodes were attached to the eye-region to monitor blinks and other eye activity. Data
were pruned to exclude any periods of off-task time (e.g., breaks), any excessively noisy
channels, and any linked channels, and were then subjected to an extended infomax
independent components analysis using EEGLAB on the SharcNet computing cluster
(ICA; Bell & Sejnowski, 1995; Makeig et al., 2004). Data were referenced offline to the
average of all sites, filtered (1-30 Hz) and all independent components representing eye
movements, heart rate, or other muscle activity were removed. All channels were then
interpolated to a standard scalp montage by spherical spline. See Desjardins and Segalowitz (2013) for further preprocessing details.

Trials were then averaged into ERP segments of 2000 ms for target tones correctly responded to in the attended and unattended ears separately, including a 200 ms prestimulus baseline. ERP group and condition differences were examined using a permutation based statistical approach described in Study 2.

The time-frequency EEG analysis was performed using the EEGLAB toolbox (Delorme & Makeig, 2004) within Matlab R2012b and used a 3-cycle wavelet with a Hanning-tapered window in order to increase resolution at higher frequencies. ERSP was determined by first computing the power spectrum (in dB) over a sliding latency window then averaging across trials within each condition separately (Delorme & Makeig, 2004). ITC was calculated by determining a spectral estimate at each time and frequency, which was then plotted as a vector on a 2-D Cartesian coordinate frame. The phase angle of the vector was examined for consistency across trials of a given condition (Delorme & Makeig, 2004). ITC values can range from 0 to 1 with values closest to 1 representing higher levels of phase coherence across trials. Alpha was set to $p < .01$ for all ITC and ERSP analyses.

**Results**

**Preliminary Analyses**

Our pre-screening measures were successful proxies of self-regulation. As can be seen in Table 4.2, BRIEF scores were significantly, and often highly correlated with Emotional Self-Regulation and Procrastination scores in the appropriate direction.
Table 4.2: Correlations between Pre-screening Measures and BRIEF Measures Collected During the Testing Session.

<table>
<thead>
<tr>
<th>BRIEF scale</th>
<th>Emotional Reactivity (ERS)</th>
<th>Difficulty with Emotion Regulation (DERS)</th>
<th>Procrastination</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRI</td>
<td>-.491**</td>
<td>-.495**</td>
<td>.691**</td>
</tr>
<tr>
<td>Inhibit</td>
<td>-.377**</td>
<td>-.350**</td>
<td>.463**</td>
</tr>
<tr>
<td>Shift</td>
<td>-.624**</td>
<td>-.512**</td>
<td>.358**</td>
</tr>
<tr>
<td>Emotional Control</td>
<td>-.780**</td>
<td>-.564**</td>
<td>.334**</td>
</tr>
<tr>
<td>Self-Monitor</td>
<td>-.347**</td>
<td>-.398**</td>
<td>.395**</td>
</tr>
<tr>
<td>MI</td>
<td>-.704**</td>
<td>-.578**</td>
<td>.466**</td>
</tr>
<tr>
<td>Initiate</td>
<td>-.412**</td>
<td>-.453**</td>
<td>.627**</td>
</tr>
<tr>
<td>Working Memory</td>
<td>-.599**</td>
<td>-.532**</td>
<td>.486**</td>
</tr>
<tr>
<td>Plan Organize</td>
<td>-.432**</td>
<td>-.439**</td>
<td>.686**</td>
</tr>
<tr>
<td>Organization of Materials</td>
<td>-.440**</td>
<td>-.450**</td>
<td>.628**</td>
</tr>
<tr>
<td>Task Monitor</td>
<td>-.355**</td>
<td>-.404**</td>
<td>.710**</td>
</tr>
<tr>
<td>GEC</td>
<td>-.624**</td>
<td>-.570**</td>
<td>.641**</td>
</tr>
</tbody>
</table>

Note: higher scores on the BRIEF represent greater self-regulation, while higher scores on the ERS and DERS represent poorer emotional self-regulation. Higher scores on the procrastination scale represent lower levels of procrastination.

**. Correlation is significant at the 0.01 level (2-tailed).

Because we selected participants based on their extreme scores on our procrastination and emotion regulation measures, all subsequent analyses utilize a similar extreme groups approach, as we cannot be sure that our participants represent a true continuum of self-regulation. Participants were divided into tertials based on their BRIEF GEC scores rather than the indirect proxies of self-regulation used in pre-screening, and the top \((M = -86.94, SD = 7.58)\) and bottom \((M = -140.90, SD = 19.10)\) tertials\(^8\) were compared on their electrocortical responses as in Study 1 \((n = 22\) per group).

Similar to Study 1 in this dissertation, the EFP was maximal at Fz, and focal analyses are conducted on this site. The N1 however was maximal at Cz, slightly more anterior to the N1 maximal of CPz in Study 1, and therefore focal analyses on the N1 are

\(^8\) These GEC raw mean scores equate to \(T\) Scores of 41 and 66, and percentile ranks of 19 and 93 respectively, according to the BRIEF-A professional manual. Thus, we were successful in selecting across the full range of self-regulatory ability.
at Cz. See Figure 4.3 for the observed N1 topography. This is consistent with prior scoring of the N1 in dual-channel auditory selective attention tasks with adults (e.g., Hillyard, Hink, Schwent, & Picton, 1973).

**Event-Related Potentials**

As can be seen in Figure 4.1, the EFP was not amplified to attended relative to unattended targets at the full sample level. When the sample was separated into tertials based on their BRIEF scores (Figure 4.2), those with the best self-regulatory skill showed an EFP amplitude difference opposite to the expected direction; that is, they showed a larger EFP to UT than AT stimuli (panel c). Poor self-regulators did not show ERP differentiation during the timing of the EFP (panel f).

*Figure 4.1. EFP at Fz collapsed across all participants. No significant AT UT EFP differences are found (panel b). Topographies in (c) depict averaged activity from 20 to 60 ms, the timing of greatest EFP amplitude.*
Moreover, N1s at Cz also did not show a significant AT UT difference, although AT UT differences were apparent after this time window. See Figure 4.3. Good and poor self-regulators did not differentiate stimulus conditions at the timing of the N1. See Figure 4.4.

Given the lack of association between our ERP measures and self-regulation at the group level, we did not continue to investigate these effects using the individual differences regression approach used in Study 1.
Figure 4.3. N1s elicited to AT and UT stimuli at Cz. (b) shows the lack of significant AT UT differentiation during this time window (the red highlighted effects are post-N1). Topographies are plotted for the N1 averaging from 75 to 125 ms, and show that the N1 is clearly maximal at Cz.

Figure 4.4. N1s as a function of BRIEF tertial and condition. Panels a, b, d and e depict ERP activation at Cz for both conditions and both groups. The remaining panels depict $p$ values for the tests of simple effects and interactions which were calculated with permutation based statistics.
Intertrial Coherence (ITC) and Event-Related Spectral Perturbation (ERSP)

As in Figure 4.5, good self-regulators showed slightly higher inter-trial coherence to UT stimuli than poor self-regulators in the mid alpha range during the late EFP (panel h). No significant group x condition interaction was uncovered (panel i).

Figure 4.5. Intertrial coherence at Fz. Note the small but significant difference in EFP ITC to UT stimuli in the good versus poor self-regulators (panel h). $p$ values have been masked for significance such that all significant effects are red, and all non-significant effects are green (panels c, f, g, h and i only).

ERSP differences at Fz were also uncovered (see Figure 4.6). Poor self-regulators had higher alpha power to ATs at Fz during the timing of the EFP than did good self-regulators (panel g). Some baseline differences were observed when comparing UT-
related ERSPs of good and poor self-regulators (panel h) but are not of concern here as no significant effects were observed in this contrast post-stimulus presentation.

Figure 4.6. ERSPs at Fz, divided by group and condition. $p$ value plots are included in the rightmost and bottom columns.

As in Figure 4.7, at the N1 we observed higher alpha ITC to ATs in the poor as compared to the good self-regulators (panel g).
Figure 4.7. ITC at Cz divided by group and condition. *p* value plots are included in the rightmost and bottom columns. N1 timing is highlighted with a black rectangle.

ERSPs also differed by group and condition (See Figure 4.8). A significant group x condition interaction was uncovered in the high alpha range (panel i). Poor self-regulators showed higher ERSP than good self-regulators to AT (panel g) but not UT stimuli (panel h) in this high alpha range. Additionally, in the mid-alpha range, poor self-regulators also showed higher ERSPs to UTs than good self-regulators during the late N1 in the simple effects (panel h). Although not a statistically significant interaction with condition, poor self-regulators showed higher levels of low-alpha/high theta ERSP to UTs than good self-regulators (panel h, effect in 4-7 Hz window). Poor self-regulators showed higher N1 related ERSP to AT rather than UT stimuli very briefly during the late N1 (panel f).
Discussion

Here we tested the hypothesis that a group of older adolescents and emerging adults differing in their real-world self-regulatory skill would also display differences in their early-occurring ERP responses during a selective auditory attention task. We analysed both scalp ERP data and spectral ITC and ERSP data in good and poor self-regulators to help answer this question.

Firstly, the EFP observed in Lackner et al. (2013, Study 1 in this dissertation) and the traditionally observed attention-sensitive N1 recorded in selective auditory attention tasks were not sensitive to stimulus conditions in the present study. The lack of an EFP...
attention effect is consistent with Lackner et al. (2013) who also did not find an attention effect in this latency when the whole sample was averaged together. Thus, the frontal activation generating the EFP does not appear to be strongly modulated by attentional differences. Surprisingly, we were unable to replicate the traditional N1 effect that is commonly observed in adult samples (see e.g., Hillyard et al., 1973; Singhal, Doerfling, & Fowler, 2002). We did not change the task from Study 1 given the clarity of the results, and the uncertainty of whether changing task parameters would influence the presence or absence of the 'newly discovered' EFP. If the EFP were not present in the older sample using different parameters we would not know if its absence was due to rates of stimulus presentation or age-related effects. Our ISIs were much longer than those that have been used by other research groups. Hillyard et al. (1973) used ISIs of 250 to 1250 ms calculated separately within each ear (meaning that stimuli could be presented at nearly twice that rate), while our stimuli were presented at an ISI of 600 to 800 ms calculated across both ears.

Such ISI differences have been shown to influence the amplitude of the N1. As ISIs increase to beyond 500ms, the N1 amplitude to sounds outside of the focal area of attention also increases, but this is perhaps due to overlapping activity generated by the previous stimuli (Davis, Mast, Yoshie, & Zerlin, 1966). The N1 at these ISIs appears to represent a novelty or orienting response to the stimuli (Atienza, Cantero, & Gómez; Näätänen & Picton, 1987; Orekhova et al., 2009), which we would expect to be larger for UT than AT stimuli. In some groups there was a trend for N1s to be larger to UT than ATs.
Moreover, the tonal difference used in the present study was much more pronounced than that used in prior work in other labs. For instance, in a similar dual-channel auditory selective attention task Nager, Estorf and Munte (2006) used tone pips that were separated by only 100Hz, while ours were separated by 1000Hz. Our much longer ISIs and more noticeable differences between the tones may have reduced task difficulty, allowing participants to perform the task in the attended ear, while still fully processing stimuli in the attended ear, leading to the observed novelty effect in the unattended ear. These task differences may explain the lack of an EFP/N1 attention effect. Given the likelihood of these explanations, we will interpret our results with respect to an auditory novelty, or oddball framework, assuming that UTs capture attention and cause an orienting response.

Although good and poor self-regulators did not show the expected AT-UT stimulus differences in their scalp ERPs, we did observe important differences between the groups in the spectral characteristics of their responses, as assessed by ERSPs and ITCs, that are in line with prior literature on the subject. Specifically, during the EFP, good self-regulators showed somewhat higher alpha ITC to UT stimuli than poor self-regulators (in the simple effects). Larger ITCs are one contributor to increased ERP amplitudes, and so this ITC effect is suggestive of increased orienting to novelty/oddballs in good self-regulators. This dovetails nicely with the larger EFPs to UTs in good rather than poor self-regulators that were observed at the scalp. Taken together, this suggests that good self-regulators are capable of performing the task in the attended ear while simultaneously paying attention to the unattended ear, and is consistent with evidence that children with ADHD experience more difficulty in dual-task situations than their
typically developing counterparts (Ewen et al., 2012). Empirical evidence for Load Theory of Selective Attention and Cognitive Control (Lavie, Hirst, deFockert & Viding, 2004) is also in agreement with these results. In situations of low perceptual load, such as that in the present investigation, spare attentional capacity can "spill-over" to the processing of irrelevant distractors. When perceptual load increases, processing of irrelevant distractors decreases (Lavie, Hirst, deFockert & Viding, 2004), and importantly these effects are not ubiquitous across the lifespan (Maylor & Lavie, 1998), suggesting that other individual difference variables (such as the ones reported here) may relate to these effects.

Poor self-regulators showed higher N1-related alpha ERSPs to attended, rather than unattended stimuli, a pattern which seems less than adaptive given a novelty interpretation. ERSPs represent the magnitude of power change which occurs post-stimulus, and poor self-regulators are having their processing perturbed by events in the attended location, and not by those tones which presumably elicit an orienting response. EEG recorded while learning to play a videogame shows that fast learners have increased alpha ERSP to important learning events compared to slow learners (Mathewson et al., 2012) and therefore salient events such as UTs (in this paradigm) should be followed by increased alpha ERSPs in the most adaptive individuals. Our poor self-regulators do not show this pattern.

Good and poor self-regulators also differed on their N1-related alpha ERSPs to attended targets, with poor self-regulators showing higher levels of alpha, a finding in agreement with Koehler et al. (2009) who report higher levels of absolute alpha power in adults with ADHD relative to controls. Thus, the spectral characteristics of good and poor
self-regulators' ERP responses differ very early on in the information processing stream at the timing of the EFP.

We additionally found some group differences in N1-related high theta ERSPs, with poor self-regulators showing higher theta ERSP to UT stimuli than did good self-regulators. Theta activity is associated with attentional orienting, and active problem solving (Başar et al., 2001; Schacter, 1977), and poor self-regulators are orienting to UTs at a later time window than our good self-regulators, who showed an alerting response during the EFP (as evidenced by the ITC differences).

Therefore, while we did not replicate the results of Study 1 using a group of older adolescents and emerging adults, this is possibly due to the lower cognitive demands of the task leading to different strategy options in this older group. Selective auditory attention tasks need to have their difficulty titrated as a function of the age of the sample. However, when we separated the effects of alpha and theta ITC and ERSPs in the scalp ERPs, we found that both had some predictive power over self-regulation. Given the paucity of research targeted at this age range, future research should investigate further the electrophysiological correlates of self-regulation in similarly aged cohorts. Doing so may help target appropriate interventions when self-regulation is impaired.
References


adolescents with attention deficit hyperactivity disorder (ADHD). *Journal of Child Psychology and Psychiatry, 51*(1), 66-76.


6. GENERAL DISCUSSION

This dissertation was designed to test a model of the predictors of self-regulatory skill in adolescence and emerging adulthood. Previous research has connected individual differences in lab-based executive functioning skill to ERPs related to error monitoring processes (Hester, Fassbender, & Garavan, 2004; Ladouceur, Dahl, & Carter, 2007), and later stages of information processing (e.g., the P300 associated with attentional orienting to novelty, Gumenyuk et al., 2005). Aside from work with clinical populations such as those with ADHD, little research has focused on the ERP correlates of day-to-day self-regulation. Here I addressed both of these gaps in the literature by focusing on ERPs related to attentional control recorded in the early stages of information processing (i.e., before 200 ms in Studies 1, 2 and 4), and self-regulation as it is manifested in day-to-day scenarios, or as Takeuchi et al. (2013) refer to them, Executive Functions during Everyday Events.

I accomplished my goals by completing four studies. In the first study I gave 12-14 year old adolescents a selective auditory attention task and asked their parents to report on their child's self-regulatory skill. Examining the ERPs related to automatic aspects of attention in relation to parental reports on the Behavior Rating Inventory of Executive Function (BRIEF) revealed that an early frontal positivity (EFP) elicited by to-be-ignored/unattended tones was larger in those with poorer self-regulation, driven by scores on the BRIEF Metacognition Index. As is traditionally found, N1 amplitudes were more negative for the to-be-attended rather than to-be-ignored/unattended tones. Additionally, N1 latencies to unattended tones correlated with parent-ratings on the BRIEF Behavior Regulation Index, where shorter latencies predicted better self-regulation. Results
suggested that the ability to disengage attention from distractor information in the early stages of stimulus processing is associated with adolescent self-regulatory skill.

These brain-behaviour associations may emerge in a number of ways. Genetic polymorphisms of psychologically relevant genes (e.g., monoamine neurotransmitter genes) may predispose some individuals to an endophenotype, i.e., an internal indirectly measurable phenotype, that can reduce or enhance the development of self-regulatory capacity. Monoamine-related genes may affect self-regulation directly, or indirectly through their influence on EEG/ERP measures of prefrontal cortex function (an endophenotype). In Study 2 I tested a model of the monoamine neurotransmitter contribution to self-regulation, investigating the hypothesis that these genes may moderate the association between ERP measures of attentional control and self-regulation. We investigated the role of dopamine (**DRD4** and **COMT**) and serotonin (**5-HTTLPR**) related genes in the relationship between EFP amplitudes and N1 latencies to unattended targets (UT) and self-regulation. We uncovered associations with dopamine-related genes. Those participants with at least one long **DRD4** VNTR allele did not differentiate between AT and UT conditions during early stimulus processing, whereas those with the short VNTR did differentiate. Thus, those who are at a lower-risk for clinical self-regulation difficulties are able to adaptively control their attention by processing attended rather than to-be-ignored information more deeply, as evidenced by early occurring ERP markers. This capacity for attentional control may then translate into better self-regulation. Those with a T allele at **DRD4** rs1800955 did not begin differentiating AT and UT stimuli at the timing of the EFP, but show differentiation during the timing of the N1. Those with the CC genotype show a reduced EFP to UT
stimuli and a reduced differentiation during the N1 relative to their T allele-carrying peers, suggesting that they have at least partially suppressed processing of UT stimuli by this time. The DRD4 rs1800955 T allele is also considered a risk allele for ADHD (see Lowe et al., 2004). Taken with my results, this suggests that risk for poor self-regulation is associated with somewhat later control of selective auditory attention (i.e., the N1 rather than the EFP).

COMT haplotypes also predicted my ERP measures. Those with a high COMT enzymatic activity haplotype did not differentiate ATs and UTs at Fz during the EFP, while those without a high COMT enzymatic haplotype had more positive AT than UT EFPs in the expected direction. Possessing a high COMT enzymatic haplotype leads to low levels of circulating dopamine, as does possessing the Val variant of the COMT rs4680 allele. Importantly, those with the Val variant of COMT rs4680 perform worse than those without the Val variant on tasks of self-regulation and executive function (Diamond, Briand, Fossella, & Gehlbach, 2004; Egan et al., 2001; Lipsky et al., 2005), a finding which is in concert with my electrophysiological results of reduced stimulus differentiation in the high COMT enzymatic activity group. However, reducing findings to conclusions based on high or low levels of circulating dopamine is misguided. Many other variables contribute to the effects that dopaminergic genes may have on behaviour, including pubertal status and the interaction of other genes. For example, Wahlstrom et al. (2007) report that an intermediate level of COMT enzymatic activity (as conferred by the Val/Met rs4680 genotype) leads to optimal performance on prefrontally mediated tasks in adolescence. I unfortunately was unable to further subdivide my relatively small sample to determine if my findings were in line with Wahlstrom et al. (2007). To my
knowledge, this is one of the only studies linking COMT haplotypes to self-regulation or related variables.

These associations were not observed for serotonergic markers (i.e., 5-HTTLPR), demonstrating a stronger contribution of the dopaminergic system than the serotonergic system to self-regulation. Prior research has connected 5-HTTLPR allele length with performance based measures of executive function in preschool aged children and adults (Canli et al., 2005; Kochanska, Philibert, & Barry, 2009). Our null results may be attributable to a weaker contribution of 5-HT to self-regulation in adolescence, or differences in genetic contributions to real-world self-regulation versus lab-based executive functioning.

Although the associations were not consistent across all measures of self-regulation, variations of DRD4 rs1800955 and COMT haplotypes predicted individual differences on the BRIEF and ASRI.

The true test of my model came when I examined whether monoamine-related genes moderated the relationship between ERPs and self-regulation, and indeed I found some support for this claim. DRD4 VNTR allele length significantly moderated the associations between N1 UT latencies and BRIEF Initiate scores, BRIEF Working Memory scores, and BRIEF MI scores, such that those without the 7-repeat allele had a negative correlation between the two variables. That is, in this group, lower self-regulation scores were associated with reduced N1 UT latencies. The associations between the BRIEF Shift subscale, the BRIEF BRI scale and the BRIEF GEC scale with EFP amplitudes to UTs were moderated by COMT haplotype status. For those participants without the high COMT enzymatic activity haplotype, larger UT amplitudes
co-occurred with higher levels of problematic self-regulatory behaviour. The moderating
effect of the COMT haplotype was also observed when examining the relationship
between N1 UT latency and self-regulation variables, namely ASRI Cognitive, Emotional
and Total scores as well as BRIEF Working Memory scores. Those adolescents with the
high COMT enzymatic activity haplotype demonstrated a positive correlation between N1
latencies and self-regulatory variables (with the exception of the Working Memory
subscale).

Without longitudinal data, the precise nature of these associations is unclear. It could
be that monoamine related genes contribute to good self-regulatory skill which in turn
influences ERP measures of attentional control, or it could be that genes influence ERP
measures of attentional control which subsequently influences self-regulation. Whether
optimal ERP regulation precedes optimal self-regulation developmentally is of theoretical
interest. Interventions should be targeted at the temporally earliest predictor of
maladjustment, and should consider individual differences in the magnitude of the
predictive effects.

In Study 3, I examined whether these parent-report measures of self-regulation
and ERP measures of attentional control were amenable to change via training in Integra
Mindfulness Martial Arts training (MMA) in a group of adolescent boys with attention-
deficit hyperactivity disorder (ADHD) and/or other self-regulatory difficulties. Parent-
report BRIEF MI scores generally improved during the period of the intervention in the
treatment, but not waitlist control group. However, there was no evidence for sustained
MI improvement during the follow-up testing session. It is possible that the intervention
may need to be longer than 20 weeks in order to be effective in the long run. This null
result may also be attributable to the small sample size at session four, and thus an underpowered analysis. Nonetheless, other research attests to the effectiveness of the MMA program (although not on an electrocortical level). Haydicky and colleagues (2012) have reported improvements to parent-rated externalizing behavior, oppositional defiance problems, conduct problems, monitoring skills and anxiety in sub-groups of MMA treatment participants that were not found for diagnosis-matched waitlist control participants.

At the group level there was no evidence for ERP change across sessions in either the treatment or control group, but a follow-up analysis indicated that the group level analyses may be masking important single-subject differences. Single-subject analyses showed that more 'optimization' of ERPs for selective auditory attention occurred in the treatment group relative to the control group. These effects were at different latencies for different individuals, suggesting that individual MMA participants benefitted from the intervention in somewhat idiosyncratic ways. We can conceptualize these individual differences loosely in terms of top-down and bottom-up processing. Today we know that attentional control can operate on both of these levels, and Study 3 presented tentative evidence for bottom-up (e.g., during the EFP) and top-down (e.g., during the P300) attentional control improvements as indexed by condition differences at these latencies in some subjects. MMA may have trained some participants to filter out information very rapidly and therefore skillfully regulate their behaviour. On the other hand, MMA may have trained other participants to attentionally intervene at later stages of information processing, and thus a prefrontal 'top-down' control of attention may be closely correlated
with self-regulation. However, further studies with paradigms that explicitly manipulate top-down and bottom-up attention are required to test this hypothesis.

Although the analyses were exploratory in nature, a tentative conclusion is that training in MMA improves some facets of regulatory skill and the neural markers of selective auditory attention. Further investigations using larger samples should verify the strength and accuracy of these results, and we are currently collecting more data with this in mind.

Growth in self-regulatory skill does not end in adolescence but continues throughout older adolescence and emerging adulthood, the term for a life stage involving continued identity development likely brought on by the prolongation of adolescence in industrialized nations (Arnett, 2000). Aside from purely societal explanations for such continued growth, physiological explanations rest on the notion that regions of the PFC important to self-regulatory skill are not fully mature until the mid-20's (Giedd, 2004). Using a gel-based EEG system I tested the hypothesis that individual differences in older adolescent's and emerging adult's self-regulatory skill would be related to ERP measures of selective auditory attention. Using a gel rather than water-based net allowed me to investigate more specifically the physiological mechanism that may be generating the effects I observed in Study 1. Larger ERP amplitudes can occur because of increased power from generator sources (here measured by ERSPs) or due to increased trial-to-trial phase consistency (ITC). We found evidence that both of these mechanisms contribute to observed associations with self-regulatory skill, although I did not find the predicted ERP effects. This null result is likely due to task parameters leading to different strategy options which can be easily altered in future research.
Thus, attentional control is related to individual differences in real-world self-regulation, during the broadly defined period of adolescence, and observed effects are at least partially moderated by allelic variants of dopaminergic genes. ERP markers of attentional control are amenable to change in populations with self-regulatory difficulties. While self-regulation clearly has many predictors, and interventions designed to improve self-regulation have idiosyncratic effects, our results help to guide personalized treatment plans where self-regulation is disordered. For example, those with the DRD4 7-repeat allele do not distinguish AT and UT conditions (Study 2), and this differentiation is related to self-regulation (Study 1). Those with the DRD4 7-repeat allele show poor self-regulation (at least on some measures – Study 2), and are at an increased risk for ADHD (e.g., Wahlstrom et al., 2007). Together this collection of findings suggests that those with a DRD4 7-repeat allele and disordered self-regulation may benefit from administration of a dopamine agonist.

Benefits of Single-Subject and Non-Parametric Bootstrapped Statistics

Perhaps owing to advances in computer technology which allow for complex computations, traditional parametric statistics (i.e., those based on standardized distributions) have seen a decrease in popularity (see Gibbons & Chakraborti, 2011; Potvin & Roff, 1993; Wilcox, 2005, for a comprehensive overview of the limitations of such tests), and non-parametric statistics based on permutation or bootstrap techniques have seen an increase in popularity. Such non-parametric statistical techniques utilize the observed data to create an empirically derived sampling distribution, rather than a theoretically driven one (which is based on the unknown parameters of the population mean and the population variance). Small departures from normality can lead to
drastically reduced power when using a parametric test (Wilcox, 2005), and robust non-parametric methods decrease the likelihood of Type I error.

Bootstrapped statistics also allow for the opportunity to test single-subject effects. That is, I can look at a particular individual to see how consistent an effect is for them, and obtain measures of effect size and statistical significance. Such single-subject effects may be masked at the group level. In Study 3 for instance, treatment effects on specific ERP components were highly variable, and would likely not be observed at the group level. Using single subject statistics I was able to see significant changes in ERPs across the treatment sessions, allowing for each subject to be their own control. Clinical research could benefit highly from such an approach.

However, along with the increased power, these techniques can be accompanied with an undesirable increase in Type I error rates when appropriate control comparisons are not made and one only looks at individual cases. However this technique can of course also help to generate hypotheses concerning appropriate treatment for the individual that can then be followed up with specific hypothesis-testing. This more specific hypothesis testing would not have an inflated alpha.

**Future Directions**

**Domain generality versus specificity.** Eminent attention researchers Anthony and Diana Deutsch were some of the first researchers to suggest that a domain-general, non-specific attention system influences multiple brain systems, with afferent and efferent connections to these regions (Deutsch & Deutsch, 1963). Modern imaging studies have partially confirmed this conjecture. Brain imaging studies suggest that the regulatory effects of attention are widespread and not limited to one isolated area of the brain.
(Posner & Raichle, 1994). Therefore, future research should not limit itself to only studying single ERP components, but should examine how widespread these associations are. At least a few reports suggest that regions of the cortex involved in very basic perceptual functions (i.e., not areas traditionally thought to be affected by attention) can show modification of activity levels as a function of attention (Kelly, Gomez-Ramirez, & Foxe, 2008). Moreover, such modulations of brain activity can be seen across a variety of sensory modalities including auditory, visual, and tactile senses (Eimer, van Velzen, & Driver, 2002; Pardo, Fox, & Raichle, 1991). Therefore, it is important to understand how domain-general or domain-specific these associations with self-regulation are. Is self-regulation only strongly associated with auditory selective attention, or is self-regulation associated with a domain-general network of attentional processes? We have already collected data from a visual selective attention task, and will be assessing the domain generality of these effects in the months to come.

**Coherence and connectivity.** Cortical networks maintain their function by means of constant activation, sometimes reflected in higher frequency EEG activity (Engel, Fries, & Singer, 2001). Coherence values indicate the magnitude of correlation between the respective amplitudes derived for a given frequency (or band) from the two time series. It is a frequency-dependent measure of the degree of linear relatedness between time series simultaneously recorded from two locations. High EEG coherence implies communication between areas of the cortex while low coherence is indicative of regional autonomy or independence (Nunez, 1995).

There is clear developmental change through adolescence in the degree of EEG phase coherence in the gamma band across frontal lobe sites, dovetailing well with existent
literature charting developmental changes in white matter during adolescence (Giorgio et al., 2008). Other measures which assess the connectivity between cortical regions are associated with behaviours related to self-regulation. Diffusion tensor imaging allows a quantification of white matter fibre tracks, critical to neural connectivity. During adolescence these measures are associated with performance on lab-based executive functioning tasks (Madsen et al., 2010; Nosarti et al., 2008). This association leads me to believe that self-regulation during adolescence might be associated with measures of EEG coherence, a likely target for future studies.

Phase reset measures can be used to assess such connectivity (Thatcher, North, & Biver, 2009). EEG activity recorded from two electrodes can either be synchronous or desynchronous with respect to phase angle. Balance between synchronization and desynchronization is essential for normal brain function. Abnormal balances are observed in epilepsy (Garcia Dominguez et al., 2005), schizophrenia (Hong et al., 2004), and Alzheimer’s disease (Stam, van der Made, Pijnenburg, & Scheltens, 2003).

Synchronization can be indexed as a stable period of phase relations called phase locking. Phase locking is thought to be important for object representation, response selection, attention and sensorimotor integration (Engel, et al., 2001). Phase synchrony enhances the saliency of neural responses, and such coordinated activity is only required to persist until that bit of information has been processed by the two neuronal populations from which the measure of phase locking is being derived. It could be important developmentally to quickly learn information and be able to move on from it.

Phase shifting, on the other hand, is observed when two neuronal populations have inconsistent differences in phase angle. During this period, they are not believed to be
communicating with one another, but rather organizing resources with other areas. Phase reset is the sum of both phase locking and phase shifting.

This measure is not static across development. Thatcher and his colleagues obtained measures of phase reset length across varying distances of the cortex from a large sample of children ages 3 months to 16 years. Interestingly a lengthening of phase shift and phase locking durations seems to occur during the adolescent period (Thatcher et al., 2009).

This set of measures has developmentally interesting psychological correlates. For example, shorter phase differences between frontal regions are associated with higher intelligence (Thatcher, North, & Biver, 2005). Moreover, longer phase locking is associated with anxiety in typically developing adolescents, while longer phase shifting is associated with aggression in this same cohort (Lackner et al., 2014).

Therefore, we presently know that this measure is associated with developmentally relevant traits, and know that it shows developmental trends, peaking around adolescence, but we know little else of its behavioural correlates, a gap in the literature that I plan on addressing in the near future. Specifically, I wish to understand whether this measure is related to self-regulation directly, or only to its correlates (e.g., behaviours related to self-regulation, variations in monoamine system functioning etc).

**General Conclusion**

Adolescence and emerging adulthood are times of continued growth in both self-regulatory skill and maturation of prefrontal cortical regions important for attentional control. The nature of this association is not fully understood. Here I examined whether self-regulation was related to markers of frontal function recorded during a selective
auditory attention task, and found evidence supporting this assertion. Self-regulation and frontal ERPs were additionally related to allelic variations in dopamine-related genes, which played a moderating relationship between the two variables. Therapeutic interventions designed to increase self-regulatory capacity are not always successful and I believe that this better understanding of the sources of variance contributing to self-regulating functions has the potential to improve the ability to identify risk factors and enhance the ability to design appropriate prevention and intervention strategies.
References


APPENDIX A

Studies 1 and 2 Participant Package
A Self-Administered Rating Scale for Pubertal Development

Directions: The next questions are about changes that may be happening to your body. These changes normally happen to different young people at different ages. Since they may have something to do with your behavior and mood, do your best to answer carefully. If you do not understand a question or do not know the answer, just mark “I don’t know.”

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Would you say that your growth in height:</td>
<td>has not yet begun to spurt</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>has barely started</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>is definitely underway</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>seems completed</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
<tr>
<td>2. Would you say that your growth in body hair:</td>
<td>has not yet begun to grow</td>
<td>1</td>
</tr>
<tr>
<td>(‘‘body hair means hair in any place other than your head, such as under your arms)</td>
<td>has barely started to grow</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>is definitely underway</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>seems completed</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
<tr>
<td>3. Have you noticed any skin changes, especially pimples?</td>
<td>skin has not yet started changing</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>skin has barely started changing</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>skin changes are definitely underway</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>skin changes seem completed</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>I don’t know</td>
<td></td>
</tr>
</tbody>
</table>

**FOR BOYS:**
4. Have you noticed a deepening of your voice?
   - voice has not yet started changing 1
   - voice has barely started changing 2
   - voice changes are definitely underway 3
   - voice changes seem completed 4
   - I don’t know

5. Have you begun to grow hair on your face?
   - facial hair has not yet started growing 1
   - facial hair has barely started growing 2
   - facial hair growth has definitely started 3
   - facial hair growth seems complete 4
   - I don’t know

**FOR GIRLS:**

4. Have you noticed that your breasts have begun to grow?
   - have not yet started growing 1
   - have barely started growing 2
   - breast growth is definitely underway 3
   - breast growth seems complete 4
   - I don’t know

5a. Have you begun to menstruate (started to have your period)?
   - yes 4
   - no 1

5b. If yes, how old were you when you started to menstruate?
   - age in years ______________
Adolescent Self-Regulation Inventory – Adolescent Self-Report Version


Read and respond to each statement. Indicate how well each describes you. Circle your answer.

<table>
<thead>
<tr>
<th></th>
<th>Not at all true for me</th>
<th>Not very true for me</th>
<th>Neither true nor untrue for me</th>
<th>Somewhat true for me</th>
<th>Really true for me</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>It’s hard for me to notice when I’ve “had enough” (sweets, food, etc.).</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>When I’m sad, I can usually start doing something that will make me feel better</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>If something isn’t going according to my plans, I change my actions to try and reach my goal.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>I can find ways to make myself study even when my friends want to go out.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>I lose track of the time when I’m doing something fun.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>When I’m bored I fidget or can’t sit still.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>It’s hard for me to get started on big projects that require planning in advance.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>I can usually act normal around everybody if I’m upset with someone.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>I am good at keeping track of lots of things going on around me, even when I’m feeling stressed.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>When I’m having a tough day, I stop myself from whining about it to my family or friends.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>11</td>
<td>I can start a new task even if I’m already tired.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>I lose control whenever I don’t get my way.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13</td>
<td>Little problems detract me from my long-term plans.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14</td>
<td>I forget about whatever else I need to do when I’m doing something really fun.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>15</td>
<td>If I really want something, I have to have it right away.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16</td>
<td>During a dull class, I have trouble forcing myself to start paying attention.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>17</td>
<td>After I’m interrupted or distracted, I can easily continue working where I left off.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>18</td>
<td>If there are other things going on around me, I find it hard to keep my attention focused on whatever I’m doing.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>19</td>
<td>I never know how much more work I have to do.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>20</td>
<td>When I have a serious disagreement with someone, I can talk calmly about it without losing control.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>21</td>
<td>It’s hard to start making plans to deal with a big project or problem, especially when I’m feeling stressed.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>22</td>
<td>I can calm myself down when I’m excited or all wound up.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>23</td>
<td>I can stay focused on my work even when it’s dull.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>24</td>
<td>I usually know when I’m going to start crying.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>25</td>
<td>I can stop myself from doing things like throwing objects when I’m mad.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>26</td>
<td>I work carefully when I know something will be tricky.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>28</td>
<td>I am usually aware of my feelings before I let them out.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>29</td>
<td>In class, I can concentrate on my work even if my friends are talking.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>30</td>
<td>When I’m excited about reaching a goal (e.g., getting my drivers license, going to college), it’s easy to start working toward it.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>31</td>
<td>I can find a way to stick with my plans and goals, even when it’s tough.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>32</td>
<td>When I have a big project, I can keep working on it.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>33</td>
<td>I can usually tell when I’m getting tired or frustrated.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>34</td>
<td>I get carried away emotionally when I get excited about something.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>35</td>
<td>I have trouble getting excited about something that’s really special when I’m tired.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>36</td>
<td>It’s hard for me to keep focused on something I find unpleasant or upsetting.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>37</td>
<td>I can resist doing something when I know I shouldn’t do it.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>42</td>
<td>I lose sleep because I worry.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>47</td>
<td>I get into arguments when people disagree with me.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>48</td>
<td>I think about the future consequences of my actions.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>53</td>
<td>I spend money without thinking about it first.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>54</td>
<td>There are days when I’m on edge all the time.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>56</td>
<td>I easily become emotionally upset when I am tired.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>57</td>
<td>Little distractions throw me off.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
58  Often I am afraid I will lose control over my feelings.

62  My mood goes up and down without a reason.

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

**The Behavior Rating Inventory of Executive Function (BRIEF)**

The BRIEF is a copyrighted questionnaire and cannot be duplicated here.
APPENDIX B

Selective Auditory Attention Task
Selective auditory attention stimulus types. In this example the participant is asked to pay attention to sounds coming in their left ear only and to supress the processing of sounds coming into their right ear. They would be asked to make a button response to high frequency (high-pitched) sounds coming in their left ear only. These four stimulus types were randomly presented to each ear in a non-overlapping fashion, at an approximate rate of one per second. AT = attended target; ANT = attended non-target; UT = unattended target; UNT = unattended non-target.
APPENDIX C

Study 2 Genetic Cross-Tabulations
<table>
<thead>
<tr>
<th></th>
<th><strong>DRD4rs1800955</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>T allele present</strong></td>
<td><strong>T allele absent</strong></td>
<td><strong>Total</strong></td>
</tr>
<tr>
<td>7-repeat present</td>
<td>9</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>7-repeat absent</td>
<td>26</td>
<td>5</td>
<td>31</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>35</td>
<td>8</td>
<td>43</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th><strong>5HTTLPR</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Low</strong></td>
<td><strong>Intermediate</strong></td>
<td><strong>High</strong></td>
</tr>
<tr>
<td>7-repeat present</td>
<td>2</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>7-repeat absent</td>
<td>8</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>10</td>
<td>21</td>
<td>10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th><strong>COMT</strong> Diplotype</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>High haplotype present</strong></td>
<td><strong>High haplotype absent</strong></td>
<td><strong>Total</strong></td>
</tr>
<tr>
<td>7-repeat present</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>7-repeat absent</td>
<td>21</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>28</td>
<td>13</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>COMT Diplotype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td>High haplotype</td>
<td>High</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td>present</td>
<td>haplotype</td>
<td></td>
</tr>
<tr>
<td>T allele present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>12</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>T allele absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>13</td>
<td>44</td>
<td></td>
</tr>
</tbody>
</table>

|                | 5HTTLPR         |         |         |         |
|                | Low             | Intermediate | High | Total   |
| T allele present|
| 11             | 17             | 9       | 37     |
| T allele absent |
| 0              | 6              | 1       | 7      |
| Total          |
| 11             | 23             | 10      | 44     |

|                | 5HTTLPR         |         |         |         |
|                | Low             | Intermediate | High | Total   |
| High haplotype present|
| 8              | 17             | 4       | 29     |
| High haplotype absent|
| 3              | 7              | 5       | 15     |
| Total          |
| 11             | 24             | 9       | 44     |
APPENDIX D

Study 4 Prescreening Measures
**Difficulties with Emotion Regulation Scale** (DERS, Gratz & Roemer, 2004).


Adaptations: (a) Original was “When I’m upset”, changed to “When I’m upset or stressed”; (b) Items 1-3 here taken from the Goals subscale; (c) Items 4-6 taken from the Strategies subscale

Please indicate how often the following statements apply to you

<table>
<thead>
<tr>
<th>Statement</th>
<th>Almost never</th>
<th>Sometimes</th>
<th>About half the time</th>
<th>Most of the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) When I’m upset or stressed, I have difficulty concentrating...</td>
<td>..○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
</tr>
<tr>
<td>b) When I’m upset or stressed, I have difficulty thinking about anything else...</td>
<td>..○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
</tr>
<tr>
<td>c) When I’m upset or stressed, I can still get things done...</td>
<td>..○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
</tr>
<tr>
<td>d) When I’m upset or stressed, I believe that wallowing in it is all I can do...</td>
<td>..○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
</tr>
<tr>
<td>e) When I’m upset or stressed, I know that I can find a way to eventually feel better...</td>
<td>..○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
</tr>
<tr>
<td>f) When I’m upset or stressed, I start to feel very bad about myself ...</td>
<td>..○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
<td>...○...</td>
</tr>
</tbody>
</table>
Emotion Reactivity Scale (Nock, Wedig, Holmberg, & Hooley, 2008).


Adaptations: (a) Deleted items 2,5,12,13,16 from Sensitivity subscale; (b) deleted items 3,17,20,21 from Intensity subscale. Kept all Persistence items.

This questionnaire asks different questions about how you experience emotions on a regular basis (for example, each day). When you are asked about being “emotional,” this may refer to being angry, sad, excited, or some other emotion. Please rate the following statements.

<table>
<thead>
<tr>
<th>Item</th>
<th>Statement</th>
<th>Likert Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>When something happens that upsets me, it’s all I can think about it for a long time</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>b)</td>
<td>My feelings get hurt easily</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>c)</td>
<td>When I experience emotions, I feel them very strongly/intensely</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>d)</td>
<td>I tend to get very emotional very easily</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>e)</td>
<td>When I feel emotional, it’s hard for me to imagine feeling any other way</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>f)</td>
<td>If I have a disagreement with someone, it takes a long time for me to get over it</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>g)</td>
<td>When I am angry/upset, it takes me much longer than most people to calm down</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>h)</td>
<td>I get angry at people very easily</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>i)</td>
<td>I am often bothered by things that other people don’t react to</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>j)</td>
<td>When something bad happens, my mood changes very quickly. People tell me I have a very short fuse</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>k)</td>
<td>People tell me that my emotions are often too intense for the situation</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>l)</td>
<td>I often get so upset it’s hard for me to think straight</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
<tr>
<td>m)</td>
<td>Other people tell me I’m overreacting</td>
<td>Not at all like me A little like me Somewhat like me A lot like me Completely like me</td>
</tr>
</tbody>
</table>
**Procrastination Scale (Tuckman, 1991)**


<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neither agree nor disagree</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) I needlessly delay finishing jobs, even when they are important</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>b) I always finish important jobs with time to spare</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>c) Whenever I make a plan of action, I follow it</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>d) I put the necessary time into even boring tasks, like studying</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>e) When I have a deadline, I wait until the last minute</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>f) I keep putting off improving my work habits</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>g) Putting something off until tomorrow is not the way I do it</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>h) I postpone starting on things I do not like to do</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>i) I delay making tough decisions</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>j) I promise myself I will do something and then drag my feet</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>k) I’m a time waster now but I can’t seem to do anything about it</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>l) When something is too tough to tackle, I believe in postponing it</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>
APPENDIX E

Ethical Clearance
Bioscience Research Ethics Board

Certificate of Ethics Clearance for Human Participant Research

DATE: 11/17/2008

PRINCIPAL INVESTIGATOR: SEGALOWITZ, Sidney - Psychology

FILE: 08-124 - SEGALOWITZ

TYPE: Faculty Research STUDENT: 

SUPERVISOR: 

TITLE: Stressed at Brock: The Brain Component

ETHICS CLEARANCE GRANTED

Type of Clearance: NEW

Expiry Date: 9/28/2012

The Brock University Bioscience Research Ethics Board has reviewed the above named research proposal and considers the procedures, as described by the applicant, to conform to the University’s ethical standards and the Tri-Council Policy Statement. Clearance granted from 11/17/2008 to 9/28/2012.

The Tri-Council Policy Statement requires that ongoing research be monitored by, at a minimum, an annual report. Should your project extend beyond the expiry date, you are required to submit a Renewal form before 9/28/2012. Continued clearance is contingent on timely submission of reports.

To comply with the Tri-Council Policy Statement, you must also submit a final report upon completion of your project. All report forms can be found on the Research Ethics web page at http://www.brocku.ca/research/policies-and-forms/research-forms.

In addition, throughout your research, you must report promptly to the REB:

a) Changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) All adverse and/or unanticipated experiences or events that may have real or potential unfavorable implications for participants;
c) New information that may adversely affect the safety of the participants or the conduct of the study;
d) Any changes in your source of funding or new funding for a previously unfunded project.

We wish you success with your research.

Approved:

Brian Roy, Chair

Bioscience Research Ethics Board

Note: Brock University is accountable for the research carried out in its own jurisdiction or under its auspices and may refuse certain research even though the REB has found it ethically acceptable.

If research participants are in the care of a health facility, at a school, or other institution or community organization, it is the responsibility of the Principal Investigator to ensure that the ethical guidelines and clearance of those facilities or institutions are obtained and filed with the REB prior to the initiation of research at that site.
To: Karen Milligan  
Psychology  
Re: REB 2012-253: Enhancing Emotion Regulation in Youth with Self-Regulation Disorders through Integra Mindfulness Martial Arts  
Date: September 7, 2012

Dear Karen Milligan,

The review of your protocol REB File REB 2012-253 is now complete. The project has been approved for a one year period. Please note that before proceeding with your project, compliance with other required University approvals/certifications, institutional requirements, or governmental authorizations may be required.

This approval may be extended after one year upon request. Please be advised that if the project is not renewed, approval will expire and no more research involving humans may take place. If this is a funded project, access to research funds may also be affected.

Please note that REB approval policies require that you adhere strictly to the protocol as last reviewed by the REB and that any modifications must be approved by the Board before they can be implemented. Adverse or unexpected events must be reported to the REB as soon as possible with an indication from the Principal Investigator as to how, in the view of the Principal Investigator, these events affect the continuation of the protocol.

Finally, if research subjects are in the care of a health facility, at a school, or other institution or community organization, it is the responsibility of the Principal Investigator to ensure that the ethical guidelines and approvals of those facilities or institutions are obtained and filed with the REB prior to the initiation of any research.

Please quote your REB file number (REB 2012-253) on future correspondence.

Congratulations and best of luck in conducting your research.

Nancy Walton, Ph.D.  
Chair, Research Ethics Board