Disentangling the effects of prenatal exposure to polysubstance on reward processing and impulsivity

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Abstract

The prenatal substance exposure has persisting effects on neurocognitive dysfunction from fetuses to children and adolescents. Among various neurocognitive functions, many studies focused on reward processing and impulsivity as they are key functions related to many psychiatric disorders. However, there were some limitations: previous studies had a relatively small sample size and the effects of prenatal polysubstance exposure were rarely investigated, even though many individuals with substance use disorders are polysubstance users. Also, the moderation effects of demographic and postnatal environmental factors were not considered in many previous studies. Here, the current study aimed 1) to replicate or further investigate the effects of prenatal exposure to each of the two most commonly used drugs (nicotine and alcohol) in a large sample, 2) to examine the effects of prenatal polysubstance exposure on reward processing and impulsivity, and 3) to investigate the influence of demographic and postnatal factors on the outcomes of prenatal drug exposure. For the goal, we used the behavioral and neuroimaging measures of reward processing and impulsivity from the Adolescent Brain Cognitive Development study in the US (N=10,161). We found that prenatal nicotine exposure was associated with hyperactivation in the inhibitory region, inferior frontal gyrus (IFG) during response inhibition. Also, we found a significant interaction effect of nicotine and alcohol on hyperactivation in ACC and IFG during response inhibition, which might indicate additive or synergistic effects of nicotine and alcohol. Lastly, we found an alteration in reward processing in the ethnically minor group and alteration in inhibitory function in children given birth from old mothers. Overall, the

results suggest that there is a need to pay close attention to the complex effects of prenatal polysubstance exposure and its interaction with demographic and postnatal factors.

Table of contents

List of Figures

1

Introduction

1.1 Substance use disorder

Substance abuse is a serious social problem. According to the National Survey of Drug Use and Health from the U.S. 2017, 51.7% of citizens aged 12 or older reported tobacco use in the past month and 17.9% reported alcohol use. Also, the Korea National Health and Nutrition Examination Survey (KNHANES) 2018 reported 22.4% of citizens aged older than 19 are currently a smoker and have smoked more than 100 cigarettes during their lifetime. Also, 60.6% have drunk alcohol more than once a month in the last year. The annual social cost of tobacco, alcohol, and illicit drug abuse in the U.S. is larger than $740 billion. Besides, the death related to drug overdose has increased almost every year since 1999 and it reached more than 67,300 death in 2018.

Substance use disorder (SUD) is a psychiatric disease where patients repetitively use addictive substances without control, despite its negative outcome. According to DSM-5, the symptoms of SUD include uncontrollable use of sub-

stances in terms of dosage and duration, craving for substances, and inability to maintain daily lives due to substances.

There are common stages of SUD; intoxication, tolerance/withdrawal, and preoccupation (Koob & Volkow, 2016). In the intoxication stage, substance activates the mesocorticolimbic dopamine pathway, where dopaminergic neurons projects from substantia nigra (SN)/ ventral tegmental area (VTA) to the striatum and the frontal lobe (Björklund & Dunnett, 2007). The release of dopamine in this pathway is related to hedonic experience. Hence, the activation of the dopamine pathway works as a positive reinforcement for repetitive drug-taking (Pierce & Kumaresan, 2006). Chronic drug users become to need a larger amount of drugs to reach the same degree of hedonic experience. This phenomenon is called tolerance and it occurs mainly due to the desensitization of the receptors that the drug of abuse binds to (Koob & Volkow, 2016). At the same time, if chronic users stop taking the drug, they experience unpleasant symptoms such as negative affect, anxiety, fatigue, and so on. This is called withdrawal symptoms. It happens because the function of the mesocorticolimbic dopamine pathway is downregulated after chronic drug use and is not properly activated anymore by natural reward (Koob & Volkow, 2016). Also, the stress system is activated during withdrawal, involving increased activation of corticotropin-releasing factor, norepinephrine, and dynorphin in basal ganglia (Koob, 2008). Therefore, abusers are preoccupied with the drug to resolve this negative state. The craving for drugs is the main characteristic of the preoccupation stage (Koob & Volkow, 2016).

Among many addictive substances, this paper focused on nicotine and alcohol, the most widely used ones. This section introduced the basic knowledge about nicotine and alcohol and its effects on neurocognitive functions, such as reward processing and impulsivity, which were commonly suggested as key

functions related to substance use disorders.

As for reward processing, the current section mainly reviewed the findings on brain activation in the ventral striatum (VS) in the Monetary incentive delay (MID) task (See Method for a detailed explanation of the task). For impulsivity, the current section covers two dimensions of impulsivity, action impulsivity, and choice impulsivity, which were measured by the stop-signal task (SST) and delay discounting task (DDT) respectively (See Method 3 for a detailed explanation of the task). For the SST, brain activation in inferior frontal gyrus (IFG) and anterior cingulate cortex (ACC) during response inhibition and stop-signal reaction time (SSRT) were included. The longer SSRT is generally interpreted as higher impulsivity.

1.1.1 Nicotine

Nicotine has a long history that tobacco has been cultivated by people in Mesoamerica dating back to 1400–1000 BC (Kaag, 2005). Nicotine is absorbed mainly by the lung and it reaches the brain in eight seconds. Then, it provides to some reinforcing effects, such as mild euphoria, increased energy, reduced stress and pain, and improved cognitive functions.

Nicotine dependence also involves three stages. In the intoxication stage, nicotine is positively reinforced by the action of nicotine at the cellular level, which binds to nicotinic acetylcholine receptors (nAChRs) and facilitates the activation of the mesocorticolimbic dopamine system (Koob & Volkow, 2016). It also reduces pain by interacting with endogenous opioids and through the suppression of inflammatory actions (Kishioka et al., 2014). In the withdrawal stage, patients show high irritability, displeasure, and high craving. This is related to the elevation of the reward threshold, which might be led by alteration in nAChRs function, decreased dopamine activity, and alterations in dopamine-

glutamate and dopamine-GABA interactions (Koob et al., 2014). Lastly, in the preoccupation stage, many patients relapse and nAChRs and corticotropin-releasing factor(CRF) play important roles. The blockade of nAChRs blocked cue-induced reinstatement and the blockade of CRF blocked stress-induced reinstatement (Koob et al., 2014).

Reward processing and impulsivity As for reward processing, one literature reviewed the anticipatory VS activation in the MID task, focusing on addicted populations. They included studies done with adults aged more than 18, addicted or at-risk populations, and traditional MID task versions (Balodis & Potenza, 2015). Here, one previous study found a diminished activation of the left VS, ACC, and right superior frontal gyrus during reward anticipation in the modified MID task (Rose et al., 2013).

For impulsivity, one previous study reported less activation of dorsal ACC in the nicotine dependence group compared to healthy control during successful inhibition in SST. The SSRT was not different between the two groups (Ruiter et al., 2012). Another study found no difference in brain activation during successful inhibition between nicotine dependents and healthy controls but found a negative association between the severity of dependence and activation of brain areas including ACC and IFG. This indicates a diminished activation in inhibitory related areas is associated with nicotine dependence. The study also could not find group differences in SSRT but find a negative association between SSRT and brain activation in areas including IFG, which implies faster stop response involves an increase in brain areas for inhibitory function (Galván et al., 2011). In the meantime, a meta-analysis reported greater delay discounting related to nicotine dependence and its severity (Amlung et al., 2017; MacKillop et al., 2011).

1.1.2 Alcohol

Alcohol also has been used for a very long time. As beer containers of 8000 BCE were discovered, it has been at least 10,000 for humans drinking alcoholic drinks (Patrick, 1952). Drinking alcohol disinhibits behavior and reduces anxiety in low blood alcohol concentration (BAC) (Cui & Koob, 2017). Therefore, it works as social lubricants or self-medication. Alcohol is absorbed within 30 to 60 minutes mainly through small intestine and stomach (Paton, 2005).

Alcoholism involves three stages like other SUDs. In the intoxication stage, the alcohol elicits sedative or anti-stress effects which involove the enhancement of inhibitory GABAergic neurotransmission and inhibition of excitatory glutamate neurotransmission. Meanwhile, it also activates a dopaminergic system in VTA as the psychostimulants do, which has positive reinforcement effects (Koob & Volkow, 2016). However, it is noteworthy that it does not mean that alcohol binds to a specific receptor. Alcohol molecule is too small to have binding energy to receptors. It rather interacts with some neuronal elements in the molecular level (Rao et al., 2015). In the withdrawal stage, abstinence of alcohol elicits the withdrawal symptom of hyper-excitability, such as tremor, increased heart rate, blood pressure, and body temperature. Psychologically, irritability, anxiety, and depression are shown in this stage. The tolerance to alcohol entails heightened metabolism of alcohol and the requirement of higher dosage to be intoxicated. The tolerance stage is related to serotonin and glutamate system as blockade of these systems blocks acute and chronic tolerance (Koob et al., 2014). For withdrawal symptoms, decreased neurotransmitter function in the VS and amygdala and decreased extracellular dopamine levels in the nucleus accumbens area play important roles (Ma & Zhu, 2014). Lastly, in the preoccupation and anticipation stage, abstinence from alcohol involves the state of

anxiety, which is related to increased CRF activity (Valdez et al., 2003).

Reward processing and impulsivity   As for reward processing, the previous studies found alcohol-dependent subjects showed decreased activation of the VS during anticipating a reward in the MID task (Beck et al., 2009; Wrase et al., 2007). The subjects did not have any other type of substance use disorder.

For impulsivity, one previous study reported no group difference in SSRT between alcohol dependence and healthy control but alcohol dependence group showed less activation of the left dorsal lateral prefrontal cortex during response inhibition. However, this study did not control nicotine dependence and not reported the number of subjects with nicotine dependence and their severity. Therefore this result may be confounded by the administration of nicotine (Li et al., 2009). In the meantime, a meta-analysis reported greater delay discounting related to alcohol dependence and its severity (Amlung et al., 2017; MacKillop et al., 2011).

1.1.3   Nicotine and alcohol

There are three possible outcomes from a combination of drugs; additive, synergistic, and antagonistic. The additive outcome means the simple addition of the effects of each drug when taken independently. The synergistic outcome means a larger effect than the additive outcome. Lastly, the antagonistic outcome refers to a smaller effect than the additive outcome (Greco & Parsons, 1995).

The co-use of nicotine and alcohol are common. The people with alcohol dependence consume twice more cigarettes compared to the general population (Falk et al., 2006). This high comorbidity might be linked to genetic, epigenetic influence, or specific pharmacokinetic interactions or counteracting mechanisms

but still more investigation is warranted (Hurley et al., 2012).

Although some studies reported the effects of the combination of nicotine and alcohol on the alteration of the cholinergic system (Ribeiro-Carvalho et al., 2009), the effects of drugs mainly converge in the mesocorticolimbic dopamine system (Doyon et al., 2013). Each increases the dopaminergic neuronal firing (Foddai et al., 2003; Gessa et al., 1985; Mameli-Engvall et al., 2006; Schilström et al., 2003). Together, they have an additive effect on enhancing dopamine release in the nucleus accumbens area (Tizabi et al., 2007).

In psycho-behavioral findings, nicotine and alcohol had an impact on the anxiety-related behavior of mice during withdrawal (Abreu-Villaça et al., 2007). Meanwhile, in one human study, alcohol and nicotine showed additive effects in some physiological measures such as increased heart rate, but nicotine also showed an antagonistic effect on slowed perceptual processing led by alcohol (PERKINS, 1997).

Reward processing and impulsivity Regarding reward processing, two previous studies investigated the difference in neural response of VS during a modified MID task in alcohol dependents who were in an alcoholism treatment program. However, all subjects were also regular smokers. They showed no neural differences while anticipating reward compared to the healthy control group. One important thing is that it should be carefully interpreted as they also met diagnostic criteria for current or lifetime abuse of other drugs such as cocaine (Bjork et al., 2008; Bjork et al., 2011).

As for impulsivity, no previous study on the relationship between the combination of nicotine and alcohol on SST and DDT were found.

1.2   The maternal substance use

Maternal substance use during pregnancy is a long-lasting challenge for public health. Approximately 10% of pregnant women reported smoking cigarettes, 4.3% having binge alcohol use in the U.S. in 2016 (National Survey on Drug Use and Health, 2016). Therefore, many researchers have paid their attention to the consequences of prenatal substance exposure on offspring and they found persisting effects on the neurological development of fetuses to children and adolescents. For example, many studies reported the increased vulnerability to psychiatric disorders including substance use disorder (Delaney-Black et al., 2011; Fisher et al., 2011; Richardson et al., 2013). Also, neurocognitive dysfunctions were associated with prenatal substance exposure in both animals and humans, from the molecular level to the brain system level.

The substance reaches to fetus across the placental barrier. The fetus can be affected by drugs in two ways; acute toxicity and teratogenic effects. The fetus is exposed to acute toxicity when the mother has a high dose of substances in the blood. The teratogenic effects refer to developmental damage caused by teratogens such as substances or viruses. Each organ has a different period of maximum teratogenic vulnerability but most of them are in between the first trimester. The brain is the most sensitive during 15-60 days after fertilization (Koob et al., 2014; Meyer & Quenzer, 2005).

This section introduced previous findings of various outcomes of prenatal exposure to nicotine and alcohol. Also, their effects on neurocognitive functions, reward processing, and impulsivity, were reviewed. As for reward processing, the current section mainly reviews two topics, first, dopaminergic reward system, and second, brain activation in the VS in the MID task. For impulsivity, the current section covers two dimensions of impulsivity, action impulsivity, and

choice impulsivity, which were measured by the SST and DDT respectively. For the SST, IFG, and ACC during response inhibition and SSRT were the focuses. Besides, for the action impulsivity of animals, diverse tasks were also included, which can be interpreted as measuring response inhibition but the tasks for hyperactivity rather than inhibition were not covered.

1.2.1 Nicotine

Nicotine exposure in utero was associated with many neurobehavioral malfunctions, supported by both animal and human studies. In rat studies, heightened locomotor activity and cognitive impairment such as attention and memory deficits are reported. In human studies, low birth weight, spontaneous abortion, sudden infant death syndrome, and impairment in motor, sensory, and cognitive ability were observed in newborns and infants exposed to nicotine. In childhood, prenatal nicotine exposure was related to an increase in externalizing behavioral problems, deficits in sustained attention, response inhibition, and memory. In adolescence, they were more vulnerable to certain psychiatric conditions such as attention-deficit/hyperactivity disorder (ADHD) and conduct disorder (ERNST et al., 2001).

Reward Processing   Prenatal exposure to nicotine impacts dopamine system and reward processing. In animal studies, it is suggested that nicotine upregulates the nicotine acetylcholine receptor in the brain of the fetus. As acetylcholine plays a critical role in the prenatal development of neurons in substantia nigra, where the neurons project to the striatum (Dwyer et al., 2009), prenatal exposure to nicotine may result in alteration in the mesolimbic dopaminergic pathway. Also, prenatal nicotine led to a lower level of dopamine release in the ventral striatum in response to nicotine in adolescent rats, which indicates a

modification of substance-specific reward function (Gold et al., 2009). A recent study examined the influence of prenatal nicotine on dopaminergic and non-dopaminergic neurons in the ventral tegmental area and it reported alterations in the intracellular signaling pathway specific to dopaminergic neurons (Keller et al., 2019), which also implicates the influence of nicotine on fetuses.

Although these studies suggested the effect of nicotine exposure on the dopamine reward system during pregnancy, it is uncertain how these molecular or cellular level alterations translate into neuro-behavioral outcomes in humans. In this regard, one human study investigated VS response to reward cue, in adolescents whose mother smoked at least one cigarette a day during pregnancy. It found that the prenatally exposed group showed a weaker ventral striatal response during reward anticipation compared to the matching control group, but no difference was found during reward receipt (Müller et al., 2013). This result indicates that the prenatal nicotine influenced the reward function in human brain as well.

Impulsivity Prenatal nicotine exposure has been associated with heightened action impulsivity. For example, the rats prenatally exposed to nicotine showed a higher frequency of anticipation response in the 5-choice serial reaction time test (5-CSRTT) (Schneider et al., 2011). In 5-CSRTT, the rats were trained to receive food by nose-poking into one of five holes when the hole was illuminated. The anticipatory response refers to a nose-poking response during intertrial intervals. As it is a failure to inhibit responses between trials, it is commonly interpreted as an index of impulsive action. Besides, during the SST, the prenatal nicotine exposed rats committed more errors and exhibited more premature behavior (Bryden et al., 2016). Here premature behavior was counted when the rats left nose-port where they were trained to wait inside it before the

beginning of every trial. While these results supported heightened action impulsivity, there was a lack of evidence that prenatal exposure to nicotine leads to impulsive choice in rats as there was no significant difference was found in the performance of the DDT between exposed group and non-exposed group (Schneider et al., 2011).

Unlike the results from animal studies, human studies provided less consistent picture. In the SST, while inhibiting already potentiated go-action, one study found weaker responses in ACC and IFG in young adults who were exposed to nicotine in utero (Holz et al., 2014), whereas two studies found greater responses in ACC and IFG (Bennett et al., 2009; Longo et al., 2013). In the mean time, the studies reported no difference in SSRT. Regarding choice impulsivity, no previous studies were found. These results pointed out the neural alteration of inhibitory function but the directionality is still ambiguous.

1.2.2 Alcohol

The most well-known outcome of prenatal exposure to alcohol is the fetal alcohol spectrum disorders (FASD) According to centers for disease control and prevention, the prevalence is 0.2 to 2 cases per 1000 live births. The small molecules of alcohol quickly pass through the placenta and reach the fetus. The damaged fetus later has low birth weight, intellectual disability, facial dysmorphology, neurodevelopmental abnormalities, and delays, which are the symptoms of FASD. Many factors interact in this process, for example, the frequency and quantity of maternal drinking, fetal developmental stage, etc. Although there are some reports that low to moderate alcohol intake has no significant relationship with FASD, the threshold of the allowable amount of alcohol is uncertain and the mechanism of FASD is still vague. There was also a study suggesting that mild, moderate, and binge drinking during pregnancy al-

tered many neuropsychological functions such as attention, cognition, language, executive function, and memory which are not necessarily equal to FASD (Flak et al., 2013). Therefore, there is no safe amount of drinks for pregnant women.

Reward Processing Many previous studies found an impact on the dopamine reward system followed by prenatal exposure to alcohol. For example, one study suggested that prenatal ethanol exposure leads to decreased excitability in dopamine neurons in the VTA (J. Wang et al., 2006). Also, it is reported that prenatal ethanol is related to a reduction in dendritic length and branching in the nucleus accumbens area, the subregion of VS where many dopamine neurons populate (Rice et al., 2012). One recent study further reported a reduction in the size of the dopamine neuron cell body in VTA and suggested the underlying mechanism of the reduction as neuroinflammation through microglia (Aghaie et al., 2020). Not only rats but also monkeys exhibited abnormal activities in striatal dopamine neurons (Valenzuela et al., 2012). In summary, animal studies support the effects of prenatal alcohol exposure on the dopamine system.

In human research, no previous study, which dealt with the reward processing of the prenatally alcohol-exposed sample, was found.

Impulsivity Similar to nicotine, prenatal exposure to alcohol also has been associated with heightened action impulsivity. In animal research, the prenatally exposed rats showed more frequent water drinking behavior in the Electro-Foot Shock Aversive Water Drinking Test (EFSDT) (Kim et al., 2013). In the task, the rats receive an electric shock whenever they lick the water for more than 5 seconds. Therefore, water drinking behavior is a lack of response inhibition even under punishment and is interpreted as action impulsivity. In another study, the more frequent premature behavior in 2-CRSTT, a modified version

of 5-CRSTT, was reported for prenatally ethanol exposed rats (R. Wang et al., 2020). Although the other study reported a contradictory result regarding 5-CRSTT (Olguin et al., 2020), the overall rat studies support the relationship between alcohol exposure and increased action impulsivity. As for choice impulsivity, however, one study reported no significant group difference in DDT (Pupe et al., 2011). Plus, the other study reported the opposite result from expectation, where fetal alcohol-exposed rats chose large delayed rewards more frequently than control did (Bañuelos et al., 2012).

In the most recent human research, the prenatally exposed group showed decreased activation in brain regions including IFG and ACC during successful inhibition (Kodali et al., 2017). However, the other studies reported increased activation in regions of ACC and frontal areas during inhibition (Fryer et al., 2007; O'Brien et al., 2013; Ware et al., 2015) but it is noteworthy that the studies looked into the neural response during all inhibition trial, rather than successful inhibition trials. Meanwhile, all of these studies reported no significant group differences in task behavioral performance, SSRT. As for delay discounting, no reference was found. To sum up, although there was some inconsistency in the detailed results, both animal and human studies found heightened impulsivity and abnormal neural activation patterns in the fetal alcohol-exposed group.

1.2.3 Nicotine and alcohol

Little is known about the interaction effect of prenatally exposed nicotine and alcohol. In rat studies, one study found a mild alteration in maternal behavior, such as less frequent touch/sniff compared to controls. It also reported lower oxytocin levels in VTA and medial preoptic areas (McMurray et al., 2008). Another research experimented with a rat model on the effects of full gestational

exposure to nicotine and alcohol simultaneously. It found no difference in many physical indices such as birth weights, eye-opening age, or weight gain but found increased nicotine self-administration. In a human study, one study reported a synergistic effect of nicotine and alcohol on preterm labor, low birth weight, and growth restriction (Odendaal et al., 2009).

The interaction of alcohol and nicotine on neurocognitive functions such as reward processing and response inhibition has not been studied to the best of our knowledge.

1.2.4 Effects of demographic and postnatal environment

The effect of prenatal exposure to alcohol and tobacco can be moderated by diverse factors such as gender, ethnicity, maternal age, maternal mental health, postnatal family environment, etc. However, little is known about the moderation effects. One study reported gender-specific effects of prenatal alcohol exposure on child mental health which was measured by Strengths and Difficulties Questionnaire (SDQ) (Sayal et al., 2007). The authors found that low levels of alcohol exposure in utero were associated with mental health problems (high SDQ score) in girls. Another study also reported a decrease in auditory and visual attention performance accuracy specifically in prenatally nicotine exposed women. However, careful interpretation is warranted as the subjects were also smokers.

The factors other than gender was also considered in some previous studies. One research examined the effects of maternal characteristics. It found old maternal age, severe alcohol-related psychosocial and physical problems of the mother, and less optimal cognitive stimulation to child moderated reduction in IQ related to prenatal alcohol exposure (Jacobson et al., 2004). The other study reported the mediation effect of emotional connection between child and

mother on the relationship between prenatal alcohol exposure and child depression symptoms (O'Connor & Paley, 2006).

However, little is known about the environmental influence on neurocognitive outcomes of prenatal exposure to nicotine and alcohol. In this regard, the current study examined the different effects of prenatal drug exposure between groups divided by gender, race and ethnicity, early life stress, maternal age, and maternal mental health.

1.3   Objectives and hypotheses

There were some limitations in previous studies. 1) The previous studies on prenatal substance exposure had a relatively small sample size, mostly under 50 people. Also, there appeared to be some inconsistency in findings. 2) The effects of prenatal polysubstance exposure did not get much attention although many people use multiple substances at the same time in a naturalistic setting. 3) Little is known about the influence of demographic, maternal, and postnatal environmental factors on the effects of prenatal drug exposure, especially on neurocognitive functions.

Therefore, the current research focused on three goals, 1) to replicate or further investigate the effects of the mono substance in utero in the large sample of more than 10,000, 2) to examine the interaction effects of polysubstance in utero, and 3) to investigate the influence of demographic and postnatal factors on the effects of prenatal drug exposure.

As for the first goal, we expect that the prenatally nicotine exposed group would show a weaker response in the VS during reward anticipation in the MID task. Also, in the SST, there would be no behavioral difference in SSRT and the neural results would be rather exploratory as previous research reported mixed

results. Whereas, there might be hypoactivation of inhibitory brain area during successful inhibition if the effects of prenatal nicotine exposure are in line with findings from nicotine dependence group. As for choice impulsivity, there would be no difference between groups. For alcohol, it is hard to make expectations for the reward processing domain due to a dearth of evidence. However, there might be weaker activation in VS if it follows the results of alcohol dependence. Also, there would be lower activation in IFG and ACC during successful inhibition in the SST with no task behavioral difference. Also, no difference in DDT is expected. Regarding the second goal, there might be additive, synergistic, or antagonistic effects of nicotine and alcohol. However, it is difficult to expect the neuro-behavioral outcomes even though we have some prior knowledge of the effects of mono substance exposure on neurocognitive functions. For the third goal, as mediation of demographic or postnatal environmental factors on the outcome of prenatal substance exposure on neurocognitive functions has not been reported, it is hard to suggest a firm hypothesis.

2

Methods

2.1 Participants

The ABCD study   This study analyzed data from the Adolescent Brain Cognitive Development (ABCD) Study. The ABCD Study is a 10-year longitudinal study following more than 10 thousand children's development, which was initiated in 2018 (Volkow et al., 2018). It is led by the National Institute of Health in the U.S. and 21 study sites over the country collaborate to collect data. All participants were aged 9 to 10 in 2018 and they were selected to represent the whole population of the U.S. in terms of demographic characteristics such as gender, ethnicity, socioeconomic status, and residential district (Garavan et al., 2018).

The main goal of this study is to identify the normal and abnormal developmental tract of the human brain. To achieve this goal, many measures are being collected, comprehensively. There are mainly seven domains, physical health, mental health, neurocognition, brain imaging, substance use, culture

& environment, and biospecimens. To measure physical health, they include anthropometrics, exercise, pubertal development, screen time, medical history, sleep pattern, and developmental history. For mental health, they conduct clinical interviews and surveys to parents and children. For neurocognition, they include many cognitive tasks like verbal learning task or flanker task. For brain imaging, they scan structural MRI, diffusion-weighted MRI, and functional MRI with tasks. Besides, they collect the data of substance use and cultural or environmental interaction of children. For biospecimens, they collect hair, baby teeth, blood, etc.

The current study   In the current study, a total of 10,161 children from the ABCD study was analyzed. Among them, 973 were exposed to nicotine in utero at least once during pregnancy. 2,074 of them were exposed to alcohol in utero at least once during pregnancy. In those children, 460 were exposed to nicotine and alcohol (see Figure 3.2).

The different number of children were excluded for each step of analysis since the number of missing values varied depending on what measures were used in at each step of analysis. The detailed sample sizes for each analysis were reported in the tables in the Appendix. Furthermore, especially for fMRI analysis, children with low imaging quality and task performance were excluded from the analysis, following the exclusion criterion suggested by the ABCD Data Analysis and Informatics Center (DAIC) (Hagler et al., 2019). Also, the fMRI data obtained from Phillips scanners were excluded based on the announcement by the ABCD study group on errors in post-processing.

2.2 Measurement

2.2.1 Demographic information

For demographic information, sex, race, interviewed age, parental education, household income, parent marriage, brain volume, data acquisition site, and children's lifetime drug use were included (see Figure 3.1). The sex was a binary variable, female or male. The race was a categorical variable, white, black, Hispanic, Asian, and others. The age was a continuous variable from 108 to 131 months. Parental education was also categorized into 21 groups, ranging from never attended/ kindergarten only to doctoral degree. The household income was categorized into 10 groups, ranging from less than $5,000 to $200,000 and greater. The parent marriage was a categorical variable, married, widowed, divorced, separated, never married, and living with a partner. The brain volume was a continuous variable of ASEG atlas ROI intracranial volume, where the unit was mm^3. There were 21 different study sites, which were categorical variables. The children's lifetime drug use was reported if there is at least one child used a certain drug. 17 drugs are included. Lastly, The MRI machine used for neuroimaging was included. There were three; GE medical systems, Philips medical systems, and Siemens. These demographic variables were used as covariates in later analysis of multiple regression to remove confounding effects on the outcome.

2.2.2 Prenatal exposure to substance

The mothers answered a retrospective survey on the developmental history of their children and it included questionnaires about maternal substance use during pregnancy. It separated the pregnancy period as before and after knowing pregnancy and collected substance use information for each period. There

were alcohol, tobacco, marijuana, cocaine/crack, heroin/morphine, and oxycontin. However, in the current paper, only alcohol and tobacco were included for analysis as they are more widely used substances compared to others. The survey asked about the daily frequency of tobacco and, for alcohol, it asked about the average drinks per week, maximum drinks in one sitting, and the number of drinks needed to feel the effects of alcohol. Yet only the average drinks per week were considered in this paper to make the measurement units comparable between substances. Finally, the current paper made a composite score for each substance by weighting 5.5/38 on the answers before knowing pregnancy and 32.5/38 on the answers after knowing pregnancy, respectively. This was based on a report that the average timing of pregnancy awareness is 5.5 weeks out of the total 38 weeks in the U.S. (Branum & Ahrens, 2017).

2.2.3 Reward processing

Monetary incentive delay task   The current study included the MID task in the ABCD study to distinguish the neurocognitive function of reward processing (Casey et al., 2018). Every trial of the task follows the same sequence. First, a cue is displayed, which is one of the five cues - Win 0.2 \$, Win 5 \$, Lose 0.2 \$, Lose 5 \$, 0 \$ (2000 ms). Then, there is an anticipation phase where participants wait until the fixation screen ends (1500–4000 ms). The researchers assume that the participants anticipate reward in the phase. After the fixation screen is removed and a target screen appears, the participants should press a button as quickly as possible to receive the reward or avoid the loss where the amount can be expected by the cue displayed at the beginning of the trial (1500-1850 ms). This is the feedback phase. The task consists of 2 runs, each with 50 trials. 10 trials for every 5 types of trials were added up to 50 trials.

By scanning the brain, the task disentangles the neural activities of anticipa-

tion and feedback phase separately. The VS has been a robust neural correlate of this task (Knutson et al., 2000). Therefore, bilateral accumbens areas, which are subregions of VS were included in the analysis as regions of interest (ROI). Also, two contrasts, anticipation of reward versus neutral, and reward positive versus neutral feedback were used.

2.2.4 Impulsivity

UPPS-P UPPS (urgency, perseverance, premeditation, and sensation seeking) is an impulsivity scale (Cyders et al., 2007; Whiteside et al., 2005). Here, a modified version from the ABCD study was used. The study group developed a short version of UPPS-P for children while considering translation to the adult version for the longitudinal study design (Barch et al., 2018). It contains 20 items and has 5 sub-scales; negative urgency, lack of premeditation, lack of perseverance, sensation-seeking, and positive urgency. The children responded on a Likert scale (4 = Not at all like me; 3 = Not like me; 2 = Somewhat like me; 1 = Very much like me) and the total score ranged from 20 to 60. The total score was included in the analysis.

Delay discounting task The delay discounting task measures choice impulsivity, where the choice of a small immediate reward is regarded as the index of higher impulsiveness and a large prolonged reward is lower impulsiveness. In the ABCD study, they used the cash choice task to measure the delay discounting tendency of children. The children answered a single question, where they were to choose between the two options; 75 dollars in 3 days (a small immediate reward) or 115 dollars in 3 months (a large prolonged reward) (Wulfert et al., 2002). The binary choice data were included in the analysis.

Stop-signal task   The ABCD study includes the SST, which measures action impulsivity or response inhibition and its neural correlates (Casey et al., 2018). Every trial of the task follows the same sequence. First, a leftward or rightward arrow cue is displayed. It is a go-signal and the participants should press a button as soon as possible when they encounter the cue. However, sometimes (in one-sixth of whole trials) suddenly an upside arrow is displayed for 300 ms after the go-signal. This is the stop-signal and the participants should withhold their responses immediately when it appears. Also, the underlying algorithm maintains 50% successful and 50% unsuccessful inhibition in stop-trials by adjusting the timing of stop-signal onset. The total length of a trial is 1000 ms. There were 2 runs, including 180 trials each. One run has 150 go-trials and 30 stop-trials.

This task measures neural activation associated with response inhibition and impulsivity. Also, as there are more go-trials, the researchers assume go-response as already potentiated behavior and the longer reaction time of stop-response is an index of impulsiveness. Therefore, the stop-signal reaction time (SSRT) was included in the analysis. For neuroimaging, two contrasts of successful inhibition phase, correct stop versus correct go, and correct stop versus incorrect stop were included in the analysis. The ACC and IFG were selected as brain regions of interests based on prior studies (Aron et al., 2004; Verbruggen & Logan, 2008).

2.2.5   Neuroimaging

In the current study, the tabulated MRI data provided by ABCD data release 2.0.1 was used for fMRI analysis. The data consists of beta values which indicate the activation strength of each ROI in certain task conditions, in the level of the individual subject. To estimate the values, the researchers first preprocessed the fMRI data and extracted ROIs after brain parcellation. They

used Desikan-Killiany Atlas and Aseg Atlas for parcellation of cortical and sub-cortical areas (Desikan et al., 2006; Fischl et al., 2002). Then, they estimated task-related ROI activation strength (beta coefficients) by fitting the general linear model. The detailed information of the MRI data acquisition and processing pipeline is elaborated in other papers (Casey et al., 2018; Hagler et al., 2019).

2.2.6 Postnatal environment

Early life stress We combined items from multiple measures in the ABCD study to make the Early Life Stress (ELS) Scale (see Appendix). The measure or surveys were answered by children or their parents. The scale included the childhood stress exposure domains suggested by the ABCD study groups; Abuse, Household Challenges, and Neglect (Hoffman et al., 2019). Abuse included Emotional and Physical Abuse. Household Challenges included five subscales, Mother Treated Violently, Household Substance Abuse, Mental Illness in the Household, Parental Separation or Divorce, and Criminal Household Member. Neglect had two subscales, Emotional and Physical Neglect. Each subscale was standardized into a z-score and the main scale scores were calculated by averaging the standardized subscale scores. The total score was calculated by averaging subscale scores. We divided groups into two, one higher than 50 percentile ELS total score and the other lower than 50 percentile ELS total score. The 50 percentile point was -0.083.

Maternal age at child birth We divided mothers into two groups. One had older age when they gave birth to their children and the other had a younger age. The cut-off age was 30, which was 50 percentile.

Maternal mental health   We included three mental conditions of biological mothers. The first was depression. If the mothers have ever suffered from depression, they were included in the depression 1 group and otherwise depression 0 group. To be more specific, the question asked whether they felt so low for a period of at least two weeks that they hardly ate or slept or couldn't work or do whatever they usually do.

The next conditions were SUD related features of the biological mothers. The mothers who have ever had at least one problem due to alcohol are categorized into SUD alcohol 1 group and otherwise alcohol 0 group. Here the problem referred to marital separation or divorce, laid off or fired from work, arrests or Driving under the influence (DUI), alcohol harmed their health, in an alcohol treatment program, suspended or expelled from school 2 or more times, isolated self from family, caused arguments or were drunk a lot.

The mothers who have ever had at least one problem due to drugs were categorized into SUD drug 1 group and otherwise drug 0 group. The list of problems was the same as alcohol's.

2.3   Analysis

2.3.1   Effects of prenatal monosubstance

Self-reported or behavioral measures   The purpose of this analysis was to investigate the group difference between mono substance exposed and no substance exposed group (independent variables) in UPPS-P, cash choice task, and SSRT (dependent variables). Thus, the children exposed to prenatal polysubstance were excluded. To examine the group difference, the effect of each substance was coded as a binary variable; 1 if the children exposed to the substance at least once during pregnancy, 0 if not exposed to any substance at

all. Each substance exposure effect for each dependent variable was tested in separate regression models while controlling for demographic variables. Every regression model was first compared with the model with only demographic variables to ensure that the prenatal exposure to a certain substance adds statistically significant amounts of explanation for the variance of dependent variables. Therefore, only those models providing a bigger R^2 value were reported. For the cash choice task, the logistic linear regression model was fitted as it is a binary variable. All linear regression models were fitted by the ordinary least square method and the influential points were removed based on Cook's distance. Also, the multicollinearity between regressors was diagnosed by a variance inflation factor (VIF) and we removed regressors with multicollinearity.

Neuroimaging   Here, we examined the group difference between mono substance exposed and no substance exposed group (independent variables) on neural activation of ROIs (dependent variables). Thus, the children exposed to prenatal polysubstance were excluded and the independent variables of substance exposure were coded as binary. Only the models providing a bigger R^2 values than control models were reported. The brain activation result was plotted by Freeview and the color differentiated t-statistics of beta coefficients. The beta coefficients were from the fitted group-level regression models and the t-statistics was computed by student t-test on the beta coefficient with the null hypothesis that the beta coefficient is zero. All group-level regression models were fitted by the ordinary least square method and influential points were removed based on Cook's distance. Also, the multicollinearity between regressors was diagnosed by a variance inflation factor (VIF) and we removed regressors with multicollinearity.

2.3.2 Effects of prenatal polysubstance

Self-reported or behavioral measures We investigated the effects of polysubstance (independent variables) on UPPS-P, cash choice task, and SSRT (dependent variables). First of all, the independent variables, substance exposure, were continuous. They were all mean-centered and standardized with 1 standard deviation. Then, the regression terms for main effects and interaction effects of the exposure severity of substances were included in the models. The models also controlled for the demographic variables. Every regression model was first compared with the control model only with demographic variables and the models providing a bigger R^2 values than the control model were reported. For the cash choice task, the logistic linear regression model was fitted. All linear regression models were fitted by the ordinary least square method and influential points were removed based on Cook's distance. Also, the multicollinearity between regressors was diagnosed by a variance inflation factor (VIF) and we removed regressors with multicollinearity.

Neuroimaging The purpose of this analysis was to investigate the effects of polysubstance (independent variables) on neural activation of ROIs (dependent variables) at the group level. The independent variables were continuous and they are first scaled. The regressors for main effects and interaction effects of polysubstance exposure were included in the models, while controlling for demographic variables. Only the models providing a bigger R^2 values than control models were reported. The brain activation result was plotted in the same manner as above. The interaction effects were also plotted by r package called 'effects', which displays the marginal effects with robust standard error (MacKinnon et al, 1985). All group-level regression models were fitted by the ordinary least square method and influential points were removed based on

Cook's distance. Also, the multicollinearity between regressors was diagnosed by a variance inflation factor (VIF) and we removed regressors with multicollinearity.

2.3.3 Propensity score matching

The effects of the mono substance and polysubstance were further tested with a newly sampled group by using propensity score matching (PSM). PSM is a statistical way to sample a group, controlling for all the variables other than one variable of interest. For mono substance analysis, the matching groups were calculated for each substance and added up to be one group at the end. For polysubstance analysis, we sampled one group with no substance exposed, matching other variables to the group with children who have ever exposed to substance prenatally. We used the MatchIt R package.

2.3.4 Effects of demographic and postnatal environment

To investigate the effects of demographic and postnatal environmental factors on the outcome of prenatal substance exposure, we repeated the analysis for polysubstance after dividing the sample into subsamples, to be specific, with or without ELS, old or young age of mothers, and with or without maternal mental health issues. Thus, we could figure out whether two subsamples show a distinctive pattern of relationships or not.

3

Results

3.1 Demographic information

The total number of children was 10,161. The demographic information included the number of children by sex, race, parental education, household income, parent's marital status, research site, children's lifetime drug use, mean brain volume size, and MRI machine used for scan (see details in Figure 3.1). Also, the number of children exposed to prenatal nicotine and alcohol divided by postnatal environmental factors are presented in Figure 3.2.

3.2 Effects of prenatal monosubstance

Reward processing There was no significant brain activation explained by nicotine or alcohol during reward anticipation and receipt phase during MID task. The result was also not significant in the PSM analysis.

		N / Mean (SD)			N / Mean (SD)
					Total = 10161
Age (month)		118.939 (7.460)		Married	7079
Sex	Female	4850		Widowed	72
	Male	5308	Parent Marriage	Divorced	893
Race	White	5428		Separated	390
	Black	1393		Never married	1100
	Hispanic	2100		Living with partner	548
	Asian	211		Site 1	367
	Other	1015		Site 2	504
Parental Education	Never attended/ kindergarten only	0		Site 3	569
				Site 4	600
	1th grade	2		Site 5	327
	2th grade	1		Site 6	486
	3th grade	10		Site 7	280
	4th grade	7		Site 8	305
	5th grade	3		Site 9	367
	6th grade	60		Site 10	649
	7th grade	19	Research Site	Site 11	367
	8th grade	52		Site 12	497
	9th grade	122		Site 13	596
	10th grade	86		Site 14	538
	11th grade	164		Site 15	336
	12th grade	155		Site 16	934
	High school graduate	831		Site 17	482
	GED or dquivalend Diploma	195		Site 18	303
				Site 19	497
	Some college	1590		Site 20	611
	Associate degree: Occupational	744		Site 21	514
				Site 22	32
	Associate degree: Academic Program	539		Alcohol	15 / 0.004 (0.246)
				Cigarette	4 / 0.002 (0.118)
	Bachelor's degree	2943		E-cigarette	8 / 0.008 (0.491)
	Master's degree	1981		Cigar	5 / 0.0004 (0.024)
	Professional School degree	303		Hookah	5 / 0.001 (0.033)
	Doctoral degree	340		Chew (smokeless tobacco)	7 / 0.001 (0.025)
Household Income	Less than $5,000	352		Pipes	5 / 0.001 (0.036)
	$5,000 - $11,999	326		Marijuana	1 / 4.92e-06 (0.0005)
	$12,000 - $15,999	219		Blunt	1 / 4.92e-06 (0.0005)
	$16,000 - $24,999	426	Lifetime Drug Use	Edible (marijuana in food)	1 / 9.84e-05 (0.010)
	$25,000 - 34,999	542			
	$35,000 - $49,999	759		Cathinones (bath salts)	1 / 9.84e-05 (0.010)
	$50,000 - $74,999	1278		Inhalant	2 / 0.001 (0.129)
	$75,000 - 99,999	1357		Amphetamine	1 / 0.001 (0.06)
	$100,000- $199,999	2921		Pills of prescription tranquilizers or sedatives	1 / 0.0004 (0.040)
	$200,000 and greater	1123			
sMRI volume (mm^3)		1514415.883 (149527.059)		Pills of prescription pain relievers	1 / 9.84e-05 (0.010)
MRI machine	GE Medical Systems	2558		Over-the-counter cough or cold medicine or DXM	2 / 0.0003 (0.022)
	Philips Medical Systems	1367			
	Siemens	6538		Other	1 / 0.004 (0.357)

Figure 3.1: The demographic information.

		N	Nicotine	Alcohol	Nicotine x Alcohol
All		10161	973	2074	460
Sex	Female	4850	467	1019	191
	Male	5308	506	1055	178
Race	White	5428	480	1433	239
	Black	1393	164	117	20
	Hispanic	2100	117	306	65
	Asian	211	4	26	3
	Other	1015	148	189	42
Earlylife stress	Low	4770	260	1062	114
	High	4431	597	869	217
Maternal age at birth	Young	5429	701	943	247
	Old	4605	263	1126	122
Maternal depression	depression 0	7683	571	1515	220
	depression 1	2117	366	469	134
Maternal SUD alcohol	SUD alcohol 0	5755	416	990	141
	SUD alcohol 1	4252	542	1060	221
Maternal SUD drug	SUD drug 0	7188	513	1442	215
	SUD drug 1	2801	445	605	151

Figure 3.2: The prenatal drug exposure and postnatal environmental information

Impulsivity Both the alcohol and nicotine group had higher UPPS-P scores compared to the not exposed group (alcohol $\beta = 0.69$, $p < 0.005$, $R^2{}_{adjusted} = 0.04$; nicotine $\beta = 0.98$, $p < 0.01$, $R^2{}_{adjusted} = 0.04$). The relationship between UPPS-P score and nicotine but not alcohol was also supported by PSM analysis ($\beta = 1.57$, $p < 0.01$, $R^2{}_{adjusted} = 0.008$). There wasn't any effect of prenatal exposure to substance on cash choice task performance and stop-signal task performance, SSRT.

For the fMRI data of the stop-signal task, the prenatally nicotine exposed group showed heightened activation in the IFG during inhibition. To be specific, bilateral pars opercularis and right pars triangularis, which are subregions of IFG, were positively activated during correct stop versus correct go contrast (right pars opercularis $t = 2.72$, $p < 0.01$; left pars opercularis $t = 2.27$, $p < 0.05$; right pars triangularis $t = 2.32$, $p < 0.05$) (Figure 3.3 A) and right pars triagularis during correct stop versus incorrect stop ($t = 2.27$, $p < 0.05$) (Figure 3.3 B). However, there was no significant effects of the alcohol group. Among these results, the association between activation in right pars opercularis and nicotine was further supported by the PSM analysis ($t = 2.25$, $p < 0.05$).

3.3   Effects of prenatal polysubstance

Reward processing In reward processing, there was no significant main effect and interaction effect of prenatal exposure to substances.

Impulsivity The severity of prenatal exposure to alcohol was significant predictor of the UPPS-P score ($\beta = 0.32$, $p < 0.05$, $R^2{}_{adjusted} = 0.04$). However, there was no significant relationship between the degree of prenatal exposure to nicotine and alcohol and other behavioral measurements such as the cash choice task performance and the SSRT.

For the fMRI analysis results, there was significant main effects of nicotine and alcohol. In the contrast of correct stop versus correct go, nicotine was associated with positive activation in multiple subregions of IFG such as bilateral pars triangularis (right $t = 2.29$, $p < 0.05$; left $t = 2.51$, $p < 0.05$), and left pars opercularis ($t = 2.17$, $p < 0.05$) in the SST (Figure 3.4 D). The activation of right pars opercularis was negatively associated with prenatal exposure to alcohol ($t = -2.23$, $p < 0.05$). Among these results, the main effects of nicotine on IFG were also significant in the PSM analysis (right pars triangularis $t = 2.12$, $p < 0.05$; left pars triangularis $t = 3.19$, $p < 0.005$; left pars opercularis $t = 3.18$, $p < 0.005$).

Besides, the interaction between nicotine and alcohol was a significant predictor of activation in IFG and ACC during inhibition. In the contrast of correct stop versus correct go, bilateral caudal cingulate gyrus (right $t = 2.26$, $p < 0.05$; left $t = 4.58$, $p < 0.001$), left pars orbitalis ($t = 3.40$, $p < 0.005$), and right pars opercularis ($t = 4.01$, $p < 0.001$) were positively associated with nicotine and alcohol interaction (Figure 3.4 A, B). Also, in correct stop versus incorrect stop, the bilateral caudal ACC (left $t = 4.92$, $p < 0.001$; right $t = 3.67$, $p < 0.001$), and left pars opercularis ($t = 5.73$, $p < 0.001$) activation increased as children were exposed to both nicotine and tobacco more frequently (Figure 3.4 C).

3.4 Effects of demographic and postnatal environment

Sex In girls, the interaction of alcohol and tobacco was associated with right caudal ACC in contrast of correct stop versus correct go during SST ($t = 2.43$, $p < 0.05$). In boys, no significant neural activation but UPPS-P and amount of alcohol exposure were positively related ($\beta = 0.49$, $p < 0.05$, $R^2_{adjusted} = 0.02$).

Race and ethnicity In white group, the interaction of alcohol and nicotine was associated with left caudal ACC in contrast of correct stop versus correct go during SST ($t = 4.39$, $p < 0.001$). In Hispanic group, UPPS-P score was positively associated with alcohol exposure ($\beta = 1.48$, $p < 0.01$, $R^2_{adjusted} = 0.04$) and negatively associated with alcohol and nicotine interaction ($t = -0.21$, $p < 0.01$). Also, as in white group, the interaction of alcohol and nicotine was associated with right caudal ACC in contrast of correct stop versus correct go during SST ($t = 2.56$, $p < 0.05$). The group responding themselves other than white, black, Hispanic and Asian showed a negative association between the activation of left accumbens area during reward receipt phase of MID task and tobacco ($t = -2.08$, $p < 0.05$) and interaction of tobacco and alcohol ($t = -2.95$, $p < 0.005$).

Maternal age at birth For the children given birth by mothers younger than 30, the interaction effects of nicotine and alcohol were observed in UPPS-P score ($\beta = 0.22$, $p < 0.005$, $R^2_{adjusted} = 0.04$). The negative association was also found in the activation of bilateral rostral ACC in the constrast of correct stop versus incorrect stop during SST (right $t = -2.31$, $p < 0.05$; left $t = -2.13$, $p < 0.05$). However, alcohol showed positive association with aforementioned impulsivity measures (UPPS-P $\beta = 0.32$, $p < 0.01$, $R^2_{adjusted} = 0.04$; right rostral ACC $t = 2.48$, $p < 0.05$; left rostral ACC $t = 2.82$, $p < 0.01$). Meanwhile, there was also negative relationship between nicotine and alcohol interaction and the activation of left accumbens area while anticipating reward during MID task ($t = -3.31$, $p < 0.005$).

For the children given birth by mothers older than 30, the main effect of alcohol showed negative relationship with multiple subregions of IFG during response inhibition. In contrast of correct stop versus correct go, right pars

opercularis ($t = -2.09$, $p < 0.05$), and, in contrast of correct stop versus incorrect stop, bilateral pars opercularis (right $t = -2.19$, $p < 0.05$; left $t = -2.14$, $p < 0.05$), and right pars triangularis ($t = -2.53$, $p < 0.05$) had negative relationships with the amount of alcohol exposure during pregnancy. In the meantime, interaction of nicotine and alcohol had a positive association with activation of the left caudal ACC during correct stop versus incorrect stop ($t = 5.19$, $p < 0.001$).

Maternal mental health   The children who have mothers with depression symptoms had no significant relationship with prenatal drug exposure and neurocognitive functions. The children who have mothers with no depression symptom showed a positive association between UPPS-P score and alcohol exposure ($\beta = 0.49$, $p < 0.001$, $R^2_{adjusted} = 0.04$) and negative association between UPPS-P score and nicotine and alcohol interaction ($\beta = -0.047$, $p < 0.05$, $R^2_{adjusted} = 0.04$). Also, there was positive association between interaction of nicotine and alcohol with beta estimates of the left caudal ACC during correct stop versus correct go condition ($t = 4.26$, $p < 0.001$).

The children with mothers who have never had a problem related to alcohol showed a negative relationship between activation of left accumbens area and interaction of nicotine and alcohol during reward anticipation in MID task ($t = -4.36$, $p < 0.001$). There was also positive relationship between activation of left caudal ACC and interaction of tobacco and alcohol in correct stop vs correct go in the SST ($t = 2.04$, $p < 0.05$) but this pattern was also observed in the children with mothers who have had problems related to alcohol at least once ($t = 4.21$, $p < 0.001$).

Both the children group with and without mothers who have had a problems related to drugs showed positive relationship between activataion of left caudal

ACC and interaction of tobacco and alcohol (without $t = 2.06$, $p < 0.05$; with $t = 3.55$, $p < 0.001$).

Early life stress The chlildren without experience of early life adversity showed negative main effects of alcohol on activation of IFG in correct stop versus incorrect stop condition in the SST (right pars opercularis $t = -2.27$, $p < 0.05$; left pars opercularis $t = -2.35$, $p < 0.05$; right pars triagnularis $t = -2.92$, $p < 0.005$; left pars opercularis $t = -2.60$, $p < 0.01$). However, the interaction effects of nicotine and alcohol was positively associated with right caudal ACC during action inhibition (correct stop versus correct go $t = 2.55$, $p < 0.05$; correct stop versus incorrect stop $t = 2.31$, $p < 0.05$). The result from the children with experience of early life adversity showed positive main effects of nicotine on bilateral pars triangularis activation in correct stop versus correct go contrast in the SST (right $t = 2.07$, $p < 0.05$; left $t = 2.80$, $p < 0.01$). There was also a positive main effect of alcohol on right rostral ACC activation during correct stop versus incorrect stop ($t = 2.08$, $p < 0.05$) and a positive interaction effect on left pars opercularis during correct stop versus correct go ($t = 2.70$, $p < 0.01$). In the meantime, there was also a negative association between left rostral ACC and interaction of nicotine and alcohol during correct stop versus incorrect stop ($t = -2.10$, $p < 0.05$).
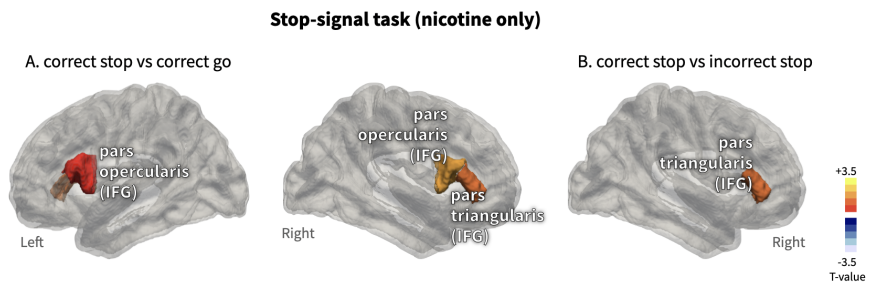
Figure 3.3: The brain activation of group exposed to only nicotine vs not exposed in the stop-signal task. The IFG was hyper-activated in prenatally nicotine exposed group during correct stop vs correctt go contrast (A) and correct stop vs incorrect stop contrast (B) ($p < 0.05$).
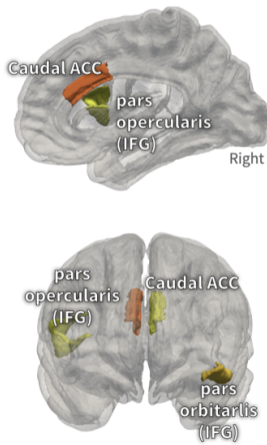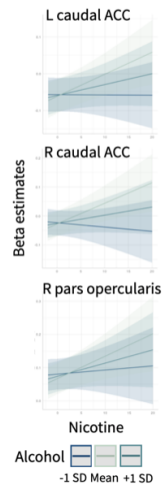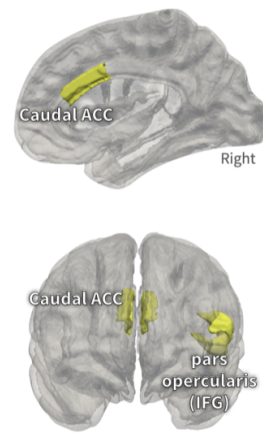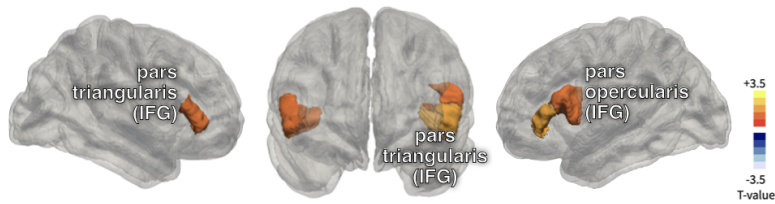
Figure 3.4: The brain activation associated with the interaction between nicotine and a combination of nicotine and alcohol exposure in utero in the stop-signal task. In the condition of correct stop versus correct go, the interaction between nicotine and alcohol was positively associated with the activation in ACC and IFG (A). The interaction plots of nicotine and alcohol in three regions (B). The interaction plots of the other regions are in the Appendix. In the condition of correct stop versus incorrect stop, the interaction between nicotine and alcohol was positively associated with the activation in ACC and IFG (C). In the condition of correct stop versus correct go, nicotine was positively associated with the activation in IFG (D), where this result was replicated in the PSM analysis.

4

Discussion

4.1 Main findings

The present study mainly aims to 1) replicate or further investigate the effects of the mono substance in utero in the large sample, 2) disentangle the effects of polysubstance in utero systematically, and 3) investigate the influence of demographic and postnatal factors on the outcomes of prenatal substance exposure. As for the first objective, the hyperactivation in IFG during successful responses inhibition was observed in children only exposed to tobacco at the fetal stage. As for the second objective, the interaction between nicotine and alcohol was turned out to be associated with hyperactivation in ACC and IFG, and nicotine to be associated with hyperactivation in IFG during response inhibition. As for the third objective, we found an alteration in reward processing (lowered activation of VS during reward anticipation) in the ethnic minority group and alteration in inhibitory function (lowered activation of IFG during successful inhibition) in children given birth from old mothers.

4.2 Interpretation on findings

4.2.1 Effects of prenatal monosubstance

Nicotine As for reward processing, prenatal exposure to nicotine was expected to show weaker VS activation during reward anticipation based on a previous study (Müller et al., 2013). However, no significant activation was reported in the current study. One possible explanation is the failure of replication. The previous study with a relatively small sample size is likely to have insufficient statistical power. Also, the age of participants in the previous study was 13 to 15, which is a distinct developmental period from 9 to 10 as it is the starting period of puberty in many people. The difference in developmental stage might lead to a null finding in the current study.

As for impulsivity, the results were consistent with expectations that there would be no difference in SSRT and DDT. However, the increased brain activation in IFG in the nicotine exposed group was not expected although it is in line with the results from two previous studies (Bennett et al., 2009; Longo et al., 2013). The two studies used different contrast not successful inhibition and the subjects with nicotine dependence showed hypoactivation in inhibitory brain areas. This result might indicate the potential elevation of inhibition function led by prenatal nicotine exposure. Considering these results together with the heightened self-reported impulsivity scale and no difference in DDT, fetal exposure to nicotine might be differentially associated with self-reported impulsivity, choice impulsivity, and action impulsivity.

These results were also supported by the PSM analysis results. It means that the effect of nicotine on self-reported impulsivity and neural activation related to action impulsivity was still significant after controlling for potential confounding factors that might not be regressed out by multiple regression due

to non-linearity.

Alcohol   For reward processing, although the alteration in dopamine system after prenatal alcohol exposure was reported in many studies, there was no significant difference in VS activity during reward processing. This might indicate that prenatal alcohol does not affect the reward processing of children.

Regarding impulsivity, the UPPS-P score was higher in the children who were at least once exposed to alcohol in utero although it was not further supported by the PSM analysis. There was no difference in DDT consistent with previous rat studies. No difference in SSRT was also expected based on prior results. However, it was not expected to observe no significant activation in IFG and ACC considering previous results (Kodali et al., 2017). Although this inconsistency might be come from a different age as mentioned above, it is also likely that the sample of the previous study lacks representativeness of population as only eight children were in the prenatally alcohol-exposed group.

4.2.2   Effects of prenatal polysubstance

To disentangle the effects of polysubstance systematically, multiple linear regression models with main effects and interaction effects of nicotine and alcohol were implemented. As for reward processing, there was no significant relationship with prenatal substance exposure and neural activation while anticipating or receiving the reward. It is noteworthy that there was no weaker VS activation in both mono substance analysis and polysubstance analysis. Even though the previous study found weaker VS activation (Beck et al., 2009; Müller et al., 2013; Rose et al., 2013; Wrase et al., 2007), the current finding implicates no significant alterations in reward processing function in the large sample.

As for impulsivity, nicotine and combination of nicotine and alcohol were

positively associated with hyperactivation of IFG during response inhibition. This result supports the hypothesis that there are additive or synergistic effects of two substances, which contributes to the greater activation of IFG. However, the directionality was not expected as lower activation of IFG was associated with slower SSRT in the SUD patients (Galván et al., 2011; Li et al., 2009; Ruiter et al., 2012) and prenatally drug-exposed group in some studies (Holz et al., 2014; Kodali et al., 2017). Furthermore, the PSM analysis only replicated the effects of nicotine, not a combination of two drugs. It indicates the possibility of non-linear confounding effects not eliminated by the statistical process of multiple linear regression.

4.2.3 Effects of demographic and postnatal environment

As for gender and impulsivity, we found both male and female group was associated with impulsivity. However, the male was more susceptible to alcohol and female was more susceptible to the combination of two drugs. Also, the only female brain was influenced by prenatal drug use. As for ethnicity, the results of the white and Hispanic group was in line with results from the total sample. However, we could not find similar results in the black and Asian groups. The size of Asians exposed to the prenatal drug was very small. However, the black group was not and it might be needed to further examine whether there are protective factors from prenatal drug exposure. The ethnic minority group, not categorized into white, black, Hispanic, or Asian, might have vulnerability to the effects of prenatal drug exposure on reward processing. They had less activation of VS while receiving reward in MID task, which was found in SUD patients (Beck et al., 2009; Müller et al., 2013; Rose et al., 2013; Wrase et al., 2007). Regarding maternal age, we found that the children delivered from old mother had decreased activation of IFG associated with alcohol exposure. The

decreased activation of IFG was also found in much previous research investigating the effects of pre/postnatal drug exposure (Galván et al., 2011; Holz et al., 2014; Kodali et al., 2017; Li et al., 2009; Ruiter et al., 2012). It might indicate malfunctioning of response inhibitory brain area, especially susceptible to prenatal alcohol exposure. For early life stress, the children located in less than 50 percentile of ELS score mainly showed a negative relationship between activation of IFG and alcohol. On the other hand, the children with more than 50 percentile ELS scores had a mainly positive relationship between nicotine exposure and IFG/ACC. The result might suggest that ELS modulates the effects of prenatal drug exposure to inhibitory brain function in different directions.

4.3   Limitations

There were some limitations to the current study. First of all, maternal substance use was self-reported. Considering social desirability bias, the possibility of fabrication or reduction in response cannot be ruled out completely. Second, the data lacks information of the absolute time point when the pregnancy was known. Although the present study summed up the values with weights based on the statistical report, there might be some deviance from true data. Also, the data lacks information on the absolute value of dosage. Since the frequency is only one index to assess the severity of substance abuse, the dosage information is needed to further validate the results in the future. Lastly, R^2 values of many regression models were extremely small (see Appendix Figure3). Thus, cautious interpretation is warranted.

4.4 Implications and further directions

To the best of my knowledge, the current study is the first study that used almost 10 thousand children to investigate the effects of prenatal substance exposure on neurocognitive functions, considering the demographic and postnatal influence at the same time. Also, when many previous studies focused on examining the clean effect of the prenatal mono substance, the current study took a different approach to examine the interaction effect of prenatal polysubstance to disentangle the complexity of it. To further scrutinize the effects of a combination of substances, controlled experiments with the animal model are needed, testing with various dosages and timing. Besides, the dynamic influence of prenatal substance exposure on different developmental phases should be studied by longitudinal follow-up. Lastly, there's the non-negligible influence of children's demographic factors, maternal factors, and postnatal environmental factors but it was not studied much. Thus, many future studies investigating those factors are needed.

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Appendix A

Supplementary

Main-scale	Sub-scale	Title of scales	Contents of questions
Abuse	Physical abuse	ABCD Youth Family Environment Scale-Family Conflict Subscale Modified from PhenX (FES)	Family members sometimes hit each other.
		ABCD Parent Diagnostic Interview for DSM-5 (KSADS) Traumatic Events	A family member threatened to kill your child
			A non-family member threatened to kill your child
			Beaten to the point of having bruises by a grown up in the home
			Shot, stabbed, or beaten brutally by a grown up in the home
			Shot, stabbed, or beaten brutally by a non-family member
			Witnessed someone shot or stabbed in the community
			Witnessed death or mass destruction in a war zone
			Witnessed or present during an act of terrorism (e.g., Boston marathon bombing)
			Witnessed or caught in a natural disaster that caused significant property damage or personal injury
			Witnessed or caught in a fire that caused significant property damage or personal injury
			Another significant accident for which your child needed specialized and intensive medical treatment
			A car accident in which your child or another person in the car was hurt bad enough to require medical attention
	Sexual abuse	ABCD Parent Diagnostic Interview for DSM-5 (KSADS) Traumatic Events	A peer forced your child to do something sexually
			An adult outside your family touched your child in his or her privates, had your child touch their privates or did other sexual things to your child
			A grown up in the home touched your child in his or her privates, had your child touch their privates, or did other sexual things to your child
Household Challenges	Mother treated violently	ABCD Parent Diagnostic Interview for DSM-5 (KSADS) Traumatic Events	Witness the grownups in the home push, shove or hit one another
	Household substance abuse	ABCD Family History Assessment Part 1	Has ANY blood relative of your child ever had any problems due to alcohol, such as: Marital separation or divorce; Laid off or fired from work; Arrests or DUIs; Alcohol harmed their health; In an alcohol treatment program; Suspended or expelled from school 2 or more times; Isolated self from family, caused arguments or were drunk a lot.
			Has ANY blood relative of your child ever had any problems due to drugs, such as: Marital separation or divorce; Laid off or fired from work; Arrests or DUIs; Drugs harmed their health; In a drug treatment program; Suspended or expelled from school 2 or more times; Isolated self from family, caused arguments or were high a lot.
		ABCD Parent Adult Self Report Scores Aseba (ASR)	I use drugs (other than alcohol, nicotine) for nonmedical purposes
			I drink too much alcohol or get drunk
			In the past 6 months, about how many times per day did you use tobacco (including smokeless tobacco)?
			In the past 6 months, on how many days were you drunk?
			In the past 6 months, on how many days did you use drugs for nonmedical purposes (including marijuana, cocaine, and other drugs, except alcohol and nicotine)?
	Mental illness in household	ABCD Family History Assessment Part 1	Has ANY blood relative of your child ever suffered from depression, that is, have they felt so low for a period of at least two weeks that they hardly ate or slept or couldn't work or do whatever they usually do?
		ABCD Family History Assessment Part 2	Has ANY blood relative of your child ever had a period of time when others were concerned because they suddenly became more active day and night and seemed not to need any sleep and talked much more than usual for them?
			Has ANY blood relative of your child ever had a period lasting six months when they saw visions or heard voices or thought people were spying on them or plotting against them?
			Has ANY blood relative of your child ever attempted or committed suicide?
		ABCD Parent Adult Self Report Raw Scores Aseba (ASR)	Depressive Problems ASR DSM-5-Oriented Scale (t score)
			Anxiety Problems ASR DSM-5-Oriented Scale (t score)
			Somatic Problems ASR DSM-5-Oriented Scale (t score)
			Avoidant Personality Problems ASR DSM-5-Oriented Scale t score)
			AD/H Problems ASR DSM-5-Oriented Scale (t score)
			Antisocial Personality Problems ASR DSM-5-Oriented Scale (t score)
			Inattention ASR DSM-5-Oriented Scale (t score)
			Hyperactivity-Impulsivity ASR DSM-5-Oriented Scale (t score)
	Parental separation or divorce	ABCD Parent Demographics Survey	Are you now married, widowed, divorced, separated, never married or living with a partner?
	Criminal household member	ABCD Family History Assessment Part 2	Has ANY blood relative of your child been the kind of person who never holds a job for long, or gets into fights, or gets into trouble with the police from time to time, or had any trouble with the law as a child or an adult?
Neglect	Emtional neglect	ABCD Children's Report of Parental Behavioral Inventory	First caregiver (caregiver participating in study/completing protocol). Makes me feel better after talking over my worries with him/her
			First caregiver (caregiver participating in study/completing protocol). Smiles at me very often.
			First caregiver (caregiver participating in study/completing protocol). Is able to make me feel better when I am upset.
			First caregiver (caregiver participating in study/completing protocol). Believes in showing his/her love for me.
			First caregiver (caregiver participating in study/completing protocol). Is easy to talk to.
			Second caregiver. Makes me feel better after talking over my worries with him/her.
			Second caregiver. Smiles at me very often.
			Second caregiver. Is able to make me feel better when I am upset.
			Second caregiver. Believes in showing his/her love for me.
			Second caregiver. Is easy to talk to.
	Physical neglect	ABCD Parental Monitoring Survey	How often do your parents/guardians know where you are?
			How often do your parents know who you are with when you are not at school and away from home?
			If you are at home when your parents or guardians are not, how often do you know how to get in touch with them?
			How often do you talk to your mom/dad or guardian about your plans for the coming day, such as your plans about what will happen at school or what you are going to do with friends?
			In an average week, how many times do you and your parents/guardians, eat dinner together?

Figure A.1: The Ealry Life Stress (ELS) scale.

UPPS-P total
R squared = 0.041   N = 8135

		Coefficient		SE	t-value
	(Intercept)	42.278	***	5.512	7.670
Prenatal	Alcohol	0.698	**	0.219	3.188
Lifetime Drug Use	Alcohol	2.640	*	1.240	2.129
	Cigarette	4.143	***	1.183	3.502
	E-cigarette	-0.622		2.717	-0.229
	Cigar	2.022		3.152	0.642
	Hookah	3.849		2.433	1.582
	Chew (smokeless tobacco)	1.145		4.095	0.280
	Pipes	-1.290		2.397	-0.538
	Blunt	-81.466		149.687	-0.544
	Cathinones (bath salts)	0.812		7.559	0.107
	Inhalant	3.369		7.504	0.449
	Pills of prescription tranquilizers or sedatives	2.803		1.864	1.503
	Pills of prescription pain relievers	9.794		7.458	1.313
	Other	-0.433	*	0.210	-2.066
	Age	-0.033	**	0.011	-2.906
Sex	Female	-2.736	***	0.190	-14.410
Race	Black	-0.079		0.334	-0.237
	Hispanic	-0.102		0.282	-0.361
	Asian	-1.055		0.623	-1.693
	Other	0.280		0.300	0.935
Parental Education	2th grade	1.283		9.149	0.140
	3th grade	4.362		6.250	0.698
	4th grade	2.194		6.104	0.359
	5th grade	11.247		7.503	1.499
	6th grade	2.512		5.415	0.464
	7th grade	1.728		5.790	0.298
	8th grade	3.051		5.513	0.553
	9th grade	3.553		5.350	0.664
	10th grade	4.771		5.391	0.885
	11th grade	2.997		5.347	0.561
	12th grade	3.237		5.339	0.606
	High school graduate	3.055		5.295	0.577
	GED or dquivalend Diploma	3.548		5.331	0.666
	Some college	2.886		5.291	0.546
	Associate degree: Occupational	2.595		5.298	0.490
	Associate degree: Academic Program	3.168		5.300	0.598
	Bachelor's degree	3.159		5.292	0.597
	Master's degree	2.626		5.294	0.496
	Professional School degree	3.538		5.312	0.666
	Doctoral degree	3.119		5.309	0.588
Household Income	$5,000 - $11,999	-0.269		0.667	-0.403
	$12,000 - $15,999	-0.009		0.738	-0.013
	$16,000 - $24,999	-0.260		0.631	-0.412
	$25,000 - 34,999	0.150		0.613	0.244
	$35,000 - $49,999	0.589		0.594	0.992
	$50,000 - $74,999	0.084		0.581	0.144
	$75,000 - 99,999	-0.630		0.596	-1.057
	$100,000- $199,999	-0.747		0.591	-1.265
	$200,000 and greater	-0.586		0.632	-0.927
Parent Marriage	Widowed	1.682		1.016	1.655
	Divorced	0.450		0.315	1.428
	Separated	-0.648		0.485	-1.336
	Never married	0.208		0.370	0.561
	Living with partner	0.157		0.432	0.364
Research Site	site 2	0.182		0.608	0.299
	site 3	-0.418		0.586	-0.713
	site 4	0.308		0.598	0.514
	site 5	2.068	**	0.678	3.050
	site 6	1.423	*	0.611	2.326
	site 7	2.979	***	0.699	4.261
	site 8	1.100		0.699	1.573
	site 9	-0.015		0.634	-0.023
	site 10	1.152	*	0.576	2.000
	site 11	0.296		0.663	0.447
	site 12	1.216		0.621	1.958
	site 13	0.282		0.594	0.475
	site 14	0.569		0.612	0.930
	site 15	1.407		0.730	1.928
	site 16	0.556		0.560	0.993
	site 17	1.705	**	0.613	2.780
	site 18	1.159		0.694	1.669
	site 19	0.278		0.621	0.448
	site 20	1.730	**	0.603	2.869
	site 21	1.188		0.611	1.945
	site 22	0.669		1.492	0.449
	sMRI volume	-0.238	*	0.109	-2.191

*** p < .001, ** p < .01, * p < .05

UPPS-P total
R squared = 0.038   N = 7065

		Coefficient		SE	t-value
	(Intercept)	42.395	***	5.615	7.550
Prenatal	Nicotine	0.981	**	0.369	2.658
Lifetime Drug Use	Alcohol	2.528		1.458	1.734
	Cigarette	4.191	***	1.199	3.496
	E-cigarette	-0.366		3.097	-0.118
	Cigar	-1.308		5.771	-0.227
	Hookah	3.724		2.533	1.470
	Chew (smokeless tobacco)	2.626		4.425	0.594
	Pipes	-2.302		2.598	-0.886
	Blunt	-80.199		151.642	-0.529
	Edible(marijuana in food)	-0.519		8.774	-0.059
	Cathinones (bath salts)	1.257		7.696	0.163
	Inhalant	1.426	*	0.581	2.452
	Pills of prescription tranquilizers or sedatives	2.898		1.890	1.533
	Pills of prescription pain relievers	9.999		7.561	1.322
	Other	-0.392		0.212	-1.850
	Age	-0.033	**	0.012	-2.640
Sex	Female	-2.477	***	0.207	-11.940
Race	Black	-0.221		0.342	-0.646
	Hispanic	-0.253		0.306	-0.826
	Asian	-1.378	*	0.677	-2.034
	Other	0.212		0.318	0.668
Parental Education	2th grade	1.188		9.274	0.128
	3th grade	2.879		6.182	0.466
	4th grade	1.961		6.188	0.317
	5th grade	11.175		7.605	1.469
	6th grade	2.278		5.485	0.415
	7th grade	1.968		5.928	0.332
	8th grade	2.808		5.563	0.505
	9th grade	2.975		5.417	0.549
	10th grade	3.268		5.448	0.600
	11th grade	2.817		5.408	0.521
	12th grade	3.305		5.411	0.611
	High school graduate	2.973		5.368	0.554
	GED or dquivalend Diploma	3.782		5.397	0.701
	Some college	2.644		5.364	0.493
	Associate degree: Occupational	2.676		5.370	0.498
	Associate degree: Academic Program	2.802		5.374	0.521
	Bachelor's degree	2.861		5.366	0.533
	Master's degree	2.267		5.368	0.422
	Professional School degree	3.667		5.393	0.680
	Doctoral degree	2.680		5.390	0.497
Household Income	$5,000 - $11,999	0.249		0.628	0.397
	$12,000 - $15,999	0.512		0.713	0.717
	$16,000 - $24,999	-0.181		0.610	-0.298
	$25,000 - 34,999	0.428		0.589	0.727
	$35,000 - $49,999	0.690		0.576	1.198
	$50,000 - $74,999	0.322		0.566	0.569
	$75,000 - 99,999	-0.645		0.587	-1.098
	$100,000- $199,999	-0.538		0.581	-0.926
	$200,000 and greater	-0.609		0.641	-0.951
Parent Marriage	Widowed	1.603		1.093	1.466
	Divorced	0.349		0.342	1.022
	Separated	-0.696		0.494	-1.410
	Never married	0.030		0.374	0.080
	Living with partner	0.096		0.440	0.217
Research Site	site 2	-0.022		0.662	-0.033
	site 3	-0.608		0.619	-0.982
	site 4	-0.008		0.631	-0.012
	site 5	2.207	**	0.739	2.986
	site 6	1.334	*	0.678	1.968
	site 7	2.816	***	0.751	3.752
	site 8	1.481		0.786	1.884
	site 9	0.137		0.695	0.197
	site 10	0.707		0.627	1.127
	site 11	0.627		0.704	0.890
	site 12	1.333	*	0.663	2.009
	site 13	0.332		0.636	0.522
	site 14	0.514		0.665	0.773
	site 15	1.478	*	0.750	1.971
	site 16	0.362		0.594	0.610
	site 17	1.877	**	0.692	2.713
	site 18	0.706		0.783	0.902
	site 19	0.066		0.662	0.100
	site 20	1.444	*	0.646	2.234
	site 21	1.383	*	0.657	2.105
	site 22	-0.003		1.906	-0.002
	sMRI volume	-0.156		0.119	-1.308

*** p < .001, ** p < .01, * p < .05

Figure A.2: The results of monosubstance analysis. UPPS-P total score and its relationship with regression variables.

SST correct stop vs cororect go, right pars triangularis N = 4195

		Coefficient	SE	t-value
	(Intercept)	-0.074	0.245	-0.301
Prenatal	Nicotine	0.036 *	0.015	2.318
Lifetime Drug Use	Alcohol	-0.113	0.136	-0.826
	Cigarette	-0.007	0.040	-0.174
	E-cigarette	-0.006	0.106	-0.053
	Cigar	0.098	0.279	0.352
	Hookah	-0.002	0.079	-0.020
	Chew (smokeless tobacco)	-0.041	0.152	-0.272
	Pipes	0.015	0.084	0.182
	Edible(marijuana in food)	0.086	0.282	0.304
	Inhalant	0.215	0.239	0.903
	Pills of prescription pain relievers	-0.150	0.236	-0.634
	Age	0.001	0.000	1.269
Sex	Female	-0.005	0.008	-0.625
Race	Black	0.007	0.015	0.479
	Hispanic	-0.026 *	0.012	-2.134
	Asian	0.014	0.029	0.478
	Other	-0.021	0.013	-1.596
Parental Education	3th grade	-0.063	0.289	-0.218
	4th grade	-0.026	0.290	-0.090
	6th grade	0.033	0.244	0.134
	7th grade	0.206	0.290	0.711
	8th grade	0.161	0.246	0.654
	9th grade	0.071	0.239	0.297
	10th grade	0.068	0.240	0.285
	11th grade	0.041	0.239	0.173
	12th grade	0.054	0.239	0.225
	High school graduate	0.109	0.237	0.459
	GED or dquivalend Diploma	0.130	0.238	0.547
	Some college	0.087	0.236	0.369
	Associate degree: Occupational	0.105	0.237	0.444
	Associate degree: Academic Program	0.080	0.237	0.339
	Bachelor's degree	0.090	0.237	0.382
	Master's degree	0.089	0.237	0.378
	Professional School degree	0.080	0.237	0.337
	Doctoral degree	0.072	0.237	0.302
Household Income	$5,000 - $11,999	-0.065 *	0.030	-2.187
	$12,000 - $15,999	0.002	0.031	0.062
	$16,000 - $24,999	-0.025	0.028	-0.876
	$25,000 - 34,999	-0.017	0.027	-0.643
	$35,000 - $49,999	-0.013	0.026	-0.498
	$50,000 - $74,999	-0.006	0.026	-0.236
	$75,000 - 99,999	0.000	0.026	0.010
	$100,000- $199,999	-0.009	0.026	-0.331
	$200,000 and greater	0.005	0.028	0.169
Parent Marriage	Widowed	-0.032	0.051	-0.625
	Divorced	0.032 *	0.014	2.233
	Separated	-0.011	0.020	-0.551
	Never married	0.039 *	0.016	2.433
	Living with partner	0.009	0.020	0.473
Research Site	site 3	0.028	0.021	1.328
	site 4	0.001	0.023	0.060
	site 5	-0.021	0.024	-0.841
	site 6	-0.016	0.021	-0.744
	site 7	-0.034	0.026	-1.318
	site 8	0.053	0.030	1.769
	site 9	-0.040	0.023	-1.733
	site 10	0.020	0.023	0.879
	site 11	-0.035	0.025	-1.416
	site 12	-0.062 **	0.021	-2.942
	site 13	-0.040	0.022	-1.818
	site 14	-0.023	0.020	-1.149
	site 15	-0.065 *	0.027	-2.448
	site 16	0.000	0.017	0.007
	site 18	-0.032	0.027	-1.175
	site 20	-0.027	0.020	-1.356
	site 21	0.004	0.021	0.204
	site 22	-0.001	0.070	-0.015
	sMRI volume	0.005	0.005	0.939

*** p < .001, ** p < .01, * p < .05

SST correct stop vs cororect go, right pars opercularis N = 4195

		Coefficient	SE	t-value
	(Intercept)	0.032	0.174	0.183
Prenatal	Nicotine	0.030 **	0.011	2.723
Lifetime Drug Use	Alcohol	-0.073	0.097	-0.758
	Cigarette	-0.028	0.028	-0.985
	E-cigarette	-0.057	0.075	-0.757
	Cigar	0.134	0.198	0.678
	Hookah	0.008	0.056	0.141
	Chew (smokeless tobacco)	0.161	0.108	1.493
	Pipes	-0.040	0.059	-0.684
	Edible(marijuana in food)	-0.197	0.200	-0.988
	Inhalant	0.200	0.169	1.183
	Pills of prescription pain relievers	-0.080	0.167	-0.477
	Age	0.000	0.000	0.844
Sex	Female	0.007	0.006	1.225
Race	Black	-0.001	0.010	-0.067
	Hispanic	-0.019 *	0.009	-2.246
	Asian	0.024	0.021	1.132
	Other	-0.022 *	0.009	-2.387
Parental Education	3th grade	-0.010	0.205	-0.051
	4th grade	-0.139	0.206	-0.675
	6th grade	0.044	0.173	0.257
	7th grade	0.289	0.205	1.409
	8th grade	0.144	0.174	0.827
	9th grade	0.069	0.169	0.409
	10th grade	0.043	0.170	0.252
	11th grade	0.061	0.169	0.359
	12th grade	0.060	0.169	0.352
	High school graduate	0.101	0.168	0.602
	GED or dquivalend Diploma	0.076	0.168	0.454
	Some college	0.083	0.167	0.494
	Associate degree: Occupational	0.094	0.168	0.563
	Associate degree: Academic Program	0.085	0.168	0.506
	Bachelor's degree	0.082	0.167	0.491
	Master's degree	0.080	0.168	0.476
	Professional School degree	0.060	0.168	0.358
	Doctoral degree	0.081	0.168	0.481
Household Income	$5,000 - $11,999	-0.040	0.021	-1.881
	$12,000 - $15,999	-0.033	0.022	-1.468
	$16,000 - $24,999	-0.038	0.020	-1.886
	$25,000 - 34,999	-0.022	0.019	-1.145
	$35,000 - $49,999	-0.040 *	0.018	-2.152
	$50,000 - $74,999	-0.022	0.018	-1.201
	$75,000 - 99,999	-0.020	0.019	-1.051
	$100,000- $199,999	-0.031	0.018	-1.650
	$200,000 and greater	-0.023	0.020	-1.138
Parent Marriage	Widowed	-0.047	0.036	-1.305
	Divorced	0.017	0.010	1.661
	Separated	-0.028 *	0.014	-1.969
	Never married	0.030 **	0.011	2.642
	Living with partner	-0.005	0.014	-0.342
Research Site	site 3	0.004	0.015	0.289
	site 4	-0.018	0.016	-1.098
	site 5	-0.020	0.017	-1.136
	site 6	-0.013	0.015	-0.880
	site 7	-0.024	0.018	-1.315
	site 8	0.008	0.021	0.355
	site 9	-0.024	0.016	-1.478
	site 10	0.003	0.016	0.175
	site 11	-0.041 *	0.017	-2.356
	site 12	-0.030 *	0.015	-1.984
	site 13	-0.057 ***	0.015	-3.709
	site 14	-0.018	0.014	-1.244
	site 15	-0.042 *	0.019	-2.244
	site 16	-0.007	0.012	-0.578
	site 18	-0.066 ***	0.019	-3.369
	site 20	-0.025	0.014	-1.800
	site 21	-0.005	0.015	-0.347
	site 22	-0.065	0.049	-1.305
	sMRI volume	0.000	0.003	0.015

*** p < .001, ** p < .01, * p < .05

Figure A.3: The results of mono substance analysis. The brain activation during SST and its relationship with regression variables.

SST correct stop vs incororect stop, right pars triangularis N = 4195

		Coefficient	SE	t-value
	(Intercept)	0.183	0.255	0.717
Prenatal	Nicotine	0.037 *	0.016	2.273
Lifetime Drug Use	Alcohol	0.021	0.142	0.150
	Cigarette	-0.017	0.041	-0.409
	E-cigarette	0.068	0.110	0.615
	Cigar	-2.084	2.457	-0.848
	Hookah	0.000	0.083	-0.003
	Chew (smokeless tobacco)	0.078	0.159	0.492
	Pipes	-0.058	0.087	-0.664
	Edible(marijuana in food)	-0.001	0.294	-0.005
	Inhalant	0.019	0.248	0.076
	Pills of prescription pain relievers	-0.044	0.246	-0.177
	Age	0.000	0.001	0.466
Sex	Female	-0.009	0.009	-1.000
Race	Black	0.020	0.015	1.305
	Hispanic	-0.025	0.013	-1.956
	Asian	0.016	0.031	0.526
	Other	-0.016	0.013	-1.187
Parental Education	3th grade	-0.373	0.301	-1.238
	4th grade	-0.102	0.302	-0.338
	6th grade	-0.307	0.254	-1.207
	7th grade	-0.223	0.302	-0.738
	8th grade	-0.164	0.256	-0.642
	9th grade	-0.206	0.249	-0.828
	10th grade	-0.191	0.250	-0.763
	11th grade	-0.186	0.249	-0.749
	12th grade	-0.181	0.249	-0.729
	High school graduate	-0.133	0.246	-0.539
	GED or dquivalend Diploma	-0.118	0.248	-0.479
	Some college	-0.164	0.246	-0.666
	Associate degree: Occupational	-0.134	0.246	-0.542
	Associate degree: Academic Program	-0.139	0.247	-0.562
	Bachelor's degree	-0.150	0.246	-0.609
	Master's degree	-0.167	0.246	-0.677
	Professional School degree	-0.154	0.247	-0.623
	Doctoral degree	-0.180	0.247	-0.728
Household Income	$5,000 - $11,999	-0.074 *	0.031	-2.383
	$12,000 - $15,999	-0.030	0.033	-0.905
	$16,000 - $24,999	-0.061 *	0.029	-2.081
	$25,000 - 34,999	-0.043	0.028	-1.565
	$35,000 - $49,999	-0.026	0.027	-0.964
	$50,000 - $74,999	-0.027	0.027	-0.992
	$75,000 - 99,999	-0.020	0.027	-0.735
	$100,000- $199,999	-0.029	0.027	-1.073
	$200,000 and greater	-0.032	0.029	-1.095
Parent Marriage	Widowed	-0.087	0.053	-1.657
	Divorced	0.012	0.015	0.823
	Separated	-0.014	0.021	-0.642
	Never married	0.004	0.017	0.212
	Living with partner	0.006	0.020	0.315
Research Site	site 3	0.022	0.022	1.001
	site 4	0.018	0.024	0.739
	site 5	-0.014	0.025	-0.560
	site 6	-0.011	0.022	-0.510
	site 7	-0.010	0.027	-0.384
	site 8	0.035	0.031	1.109
	site 9	-0.068 **	0.024	-2.847
	site 10	0.023	0.024	0.953
	site 11	-0.015	0.026	-0.572
	site 12	-0.036	0.022	-1.648
	site 13	-0.018	0.023	-0.776
	site 14	0.010	0.021	0.458
	site 15	-0.022	0.028	-0.785
	site 16	-0.004	0.018	-0.217
	site 18	0.013	0.029	0.468
	site 20	-0.014	0.021	-0.692
	site 21	0.005	0.022	0.232
	site 22	0.010	0.073	0.132
	sMRI volume	0.000	0.005	-0.002

*** p < .001, ** p < .01, * p < .05

SST correct stop vs cororect go, left pars opercularis N = 4195

		Coefficient	SE	t-value
	(Intercept)	0.036	0.166	0.217
Prenatal	Nicotine	0.021 *	0.010	1.987
Lifetime Drug Use	Alcohol	-0.115	0.092	-1.247
	Cigarette	0.000	0.027	-0.001
	E-cigarette	-0.007	0.072	-0.093
	Cigar	-0.620	1.595	-0.389
	Hookah	-0.045	0.054	-0.832
	Chew (smokeless tobacco)	0.106	0.103	1.033
	Pipes	-0.040	0.057	-0.708
	Edible(marijuana in food)	-0.215	0.191	-1.126
	Inhalant	0.326 *	0.161	2.020
	Pills of prescription pain relievers	-0.110	0.160	-0.692
	Age	0.000	0.000	-0.584
Sex	Female	-0.008	0.006	-1.430
Race	Black	0.016	0.010	1.580
	Hispanic	-0.014	0.008	-1.712
	Asian	0.018	0.020	0.883
	Other	-0.016	0.009	-1.840
Parental Education	3th grade	-0.017	0.196	-0.084
	4th grade	0.007	0.196	0.036
	6th grade	0.079	0.165	0.477
	7th grade	0.268	0.196	1.368
	8th grade	0.127	0.166	0.765
	9th grade	0.099	0.162	0.613
	10th grade	0.070	0.162	0.432
	11th grade	0.085	0.161	0.527
	12th grade	0.096	0.162	0.592
	High school graduate	0.094	0.160	0.585
	GED or dquivalend Diploma	0.088	0.161	0.550
	Some college	0.073	0.160	0.460
	Associate degree: Occupational	0.082	0.160	0.510
	Associate degree: Academic Program	0.077	0.160	0.478
	Bachelor's degree	0.076	0.160	0.478
	Master's degree	0.074	0.160	0.464
	Professional School degree	0.067	0.161	0.419
	Doctoral degree	0.090	0.161	0.563
Household Income	$5,000 - $11,999	-0.042 *	0.020	-2.106
	$12,000 - $15,999	-0.030	0.021	-1.398
	$16,000 - $24,999	-0.036	0.019	-1.864
	$25,000 - 34,999	-0.007	0.018	-0.375
	$35,000 - $49,999	-0.023	0.018	-1.287
	$50,000 - $74,999	-0.012	0.017	-0.703
	$75,000 - 99,999	-0.005	0.018	-0.283
	$100,000- $199,999	-0.020	0.018	-1.154
	$200,000 and greater	-0.015	0.019	-0.759
Parent Marriage	Widowed	-0.034	0.034	-1.001
	Divorced	0.014	0.010	1.467
	Separated	-0.021	0.014	-1.497
	Never married	0.027 *	0.011	2.494
	Living with partner	0.004	0.013	0.305
Research Site	site 3	0.013	0.014	0.890
	site 4	0.007	0.016	0.443
	site 5	-0.029	0.016	-1.767
	site 6	-0.011	0.014	-0.752
	site 7	-0.020	0.017	-1.146
	site 8	-0.025	0.020	-1.218
	site 9	-0.011	0.016	-0.729
	site 10	0.007	0.015	0.438
	site 11	-0.032	0.017	-1.937
	site 12	-0.025	0.014	-1.770
	site 13	-0.015	0.015	-0.996
	site 14	-0.014	0.014	-1.034
	site 15	-0.026	0.018	-1.469
	site 16	-0.003	0.012	-0.264
	site 18	-0.028	0.019	-1.506
	site 20	0.007	0.013	0.506
	site 21	0.003	0.014	0.188
	site 22	-0.019	0.047	-0.411
	sMRI volume	0.000	0.003	0.099

*** p < .001, ** p < .01, * p < .05

Figure A.4: The results of mono substance analysis. The brain activation during SST and its relationship with regression variables.

UPPS-P total				
R squared = 0.041				N = 8975
		Coefficient	SE	t-value
	(Intercept)	41.894 ***	5.528	7.579
	Nicotine	0.101 ***	0.082	1.225
Prenatal	Alcohol	0.316 ***	0.137	2.309
	Nicotine x Alcohol	-0.058 ***	0.032	-1.822
	Alcohol	2.299	1.215	1.892
	Cigarette	4.226 ***	1.177	3.589
	E-cigarette	0.419 **	0.156	2.690
	Cigar	1.933	3.171	0.610
	Hookah	3.747	2.386	1.571
	Chew (smokeless tobacco)	0.866	4.122	0.210
Lifetime	Pipes	-1.266	2.412	-0.525
Drug Use	Blunt	-81.694	150.596	-0.542
	Edible(marijuana in food)	1.675	8.576	0.195
	Cathinones (bath salts)	1.195	7.606	0.157
	Inhalant	1.396 *	0.577	2.417
	Pills of prescription tranquilizers or sedatives	2.784	1.878	1.483
	Pills of prescription pain relievers	9.714	7.510	1.294
	Other	-0.388	0.210	-1.846
	Age	-0.032 **	0.011	-2.986
Sex	Female	-2.650 ***	0.182	-14.525
	Black	-0.247	0.313	-0.790
Race	Hispanic	-0.152	0.268	-0.568
	Asian	-1.032	0.618	-1.669
	Other	0.321	0.282	1.140
	2th grade	1.552	9.211	0.169
	3th grade	3.093	6.140	0.504
	4th grade	2.428	6.144	0.395
	5th grade	11.664	7.549	1.545
	6th grade	2.495	5.448	0.458
	7th grade	1.962	5.828	0.337
	8th grade	2.693	5.513	0.488
	9th grade	3.338	5.378	0.621
	10th grade	3.451	5.402	0.639
Parental	11th grade	3.336	5.365	0.622
Education	12th grade	3.423	5.369	0.638
	High school graduate	3.432	5.329	0.644
	GED or dquivalend Diploma	4.483	5.354	0.837
	Some college	3.264	5.325	0.613
	Associate degree: Occupational	3.068	5.331	0.576
	Associate degree: Academic Program	3.361	5.333	0.630
	Bachelor's degree	3.331	5.327	0.625
	Master's degree	2.805	5.328	0.526
	Professional School degree	3.713	5.346	0.695
	Doctoral degree	3.286	5.343	0.615
	$5,000 - $11,999	0.129	0.607	0.213
	$12,000 - $15,999	0.364	0.681	0.534
	$16,000 - $24,999	-0.077	0.582	-0.133
Household	$25,000 - 34,999	0.549	0.561	0.979
Income	$35,000 - $49,999	0.735	0.548	1.342
	$50,000 - $74,999	0.271	0.535	0.507
	$75,000 - 99,999	-0.331	0.551	-0.602
	$100,000- $199,999	-0.515	0.547	-0.941
	$200,000 and greater	-0.314	0.590	-0.531
	Widowed	1.255	0.966	1.300
Parent	Divorced	0.513	0.297	1.729
Marriage	Separated	-0.666	0.447	-1.488
	Never married	0.350	0.339	1.032
	Living with partner	0.368	0.390	0.945
	site 2	0.294	0.589	0.499
	site 3	-0.238	0.572	-0.416
	site 4	0.233	0.573	0.406
	site 5	2.183 ***	0.653	3.345
	site 6	1.591 **	0.594	2.678
	site 7	2.966 ***	0.676	4.385
	site 8	1.098	0.690	1.592
	site 9	-0.010	0.623	-0.017
	site 10	1.142 *	0.563	2.027
	site 11	0.551	0.635	0.868
Research	site 12	1.175	0.603	1.948
Site	site 13	0.285	0.575	0.495
	site 14	0.694	0.592	1.172
	site 15	1.631 *	0.672	2.428
	site 16	0.479	0.546	0.876
	site 17	1.801 **	0.599	3.006
	site 18	1.531 *	0.670	2.285
	site 19	0.290	0.603	0.482
	site 20	1.793 **	0.583	3.073
	site 21	1.265 *	0.592	2.137
	site 22	0.537	1.474	0.364
	sMRI volume	-0.222 *	0.104	-2.123

*** p < .001, ** p < .01, * p < .05

Figure A.5: The results of the polysubstance analysis. UPPS-P total score and its relationship with regression variables.

SST correct stop vs correct go, left caudal ACC — N = 5336

		Coefficient	SE	t-value
	(Intercept)	-0.053	0.166	-0.319
Prenatal	Nicotine	0.003	0.002	1.285
	Alcohol	-0.002	0.003	-0.729
	Nicotine x Alcohol	0.003 ***	0.001	4.584
Lifetime Drug Use	Alcohol	-0.036	0.043	-0.838
	Cigarette	1.077	1.093	0.986
	E-cigarette	-0.054	0.072	-0.751
	Cigar	0.123	0.076	1.612
	Hookah	-0.040	0.054	-0.748
	Chew (smokeless tobacco)	0.062	0.090	0.688
	Pipes	-0.031	0.055	-0.562
	Edible(marijuana in food)	-0.008	0.185	-0.044
	Inhalant	0.227	0.162	1.398
	Pills of prescription pain relievers	0.021	0.161	0.133
	Age	0.000	0.000	-0.181
Sex	Female	0.004	0.005	0.721
Race	Black	0.017	0.009	1.784
	Hispanic	-0.008	0.007	-1.100
	Asian	0.011	0.018	0.623
	Other	-0.013	0.008	-1.597
Parental Education	3th grade	0.001	0.197	0.007
	4th grade	0.048	0.198	0.244
	6th grade	0.084	0.166	0.508
	7th grade	0.262	0.186	1.411
	8th grade	0.146	0.167	0.874
	9th grade	0.150	0.163	0.919
	10th grade	0.160	0.163	0.983
	11th grade	0.143	0.162	0.883
	12th grade	0.135	0.162	0.834
	High school graduate	0.146	0.161	0.905
	GED or dquivalend Diploma	0.156	0.162	0.963
	Some college	0.133	0.161	0.827
	Associate degree: Occupational	0.136	0.161	0.845
	Associate degree: Academic Program	0.126	0.161	0.785
	Bachelor's degree	0.130	0.161	0.805
	Master's degree	0.123	0.161	0.765
	Professional School degree	0.121	0.161	0.751
	Doctoral degree	0.135	0.161	0.835
Household Income	$5,000 - $11,999	-0.056 **	0.020	-2.869
	$12,000 - $15,999	-0.011	0.021	-0.537
	$16,000 - $24,999	-0.042 *	0.019	-2.274
	$25,000 - 34,999	0.002	0.017	0.116
	$35,000 - $49,999	-0.010	0.017	-0.571
	$50,000 - $74,999	-0.011	0.017	-0.626
	$75,000 - 99,999	0.008	0.017	0.486
	$100,000- $199,999	-0.009	0.017	-0.513
	$200,000 and greater	0.000	0.018	-0.024
Parent Marriage	Widowed	-0.020	0.030	-0.689
	Divorced	0.008	0.008	0.956
	Separated	-0.008	0.013	-0.637
	Never married	0.026 *	0.010	2.532
	Living with partner	0.002	0.012	0.135
Research Site	site 3	0.014	0.013	1.090
	site 4	0.008	0.014	0.590
	site 5	-0.014	0.014	-0.985
	site 6	-0.009	0.012	-0.744
	site 7	0.004	0.015	0.240
	site 8	0.000	0.017	-0.023
	site 9	-0.016	0.014	-1.162
	site 10	0.011	0.013	0.791
	site 11	-0.017	0.015	-1.124
	site 12	-0.020	0.013	-1.577
	site 13	-0.015	0.013	-1.139
	site 14	0.003	0.012	0.257
	site 15	-0.012	0.016	-0.767
	site 16	0.003	0.010	0.248
	site 18	0.000	0.015	-0.031
	site 20	-0.011	0.012	-0.907
	site 21	0.000	0.012	0.001
	site 22	-0.001	0.038	-0.019
	sMRI volume	0.002	0.003	0.739

*** p < .001, ** p < .01, * p < .05

SST correct stop vs correct go, right caudal ACC — N = 5336

		Coefficient	SE	t-value
	(Intercept)	-0.019	0.163	-0.114
Prenatal	Nicotine	0.003	0.002	1.269
	Alcohol	-0.002	0.003	-0.876
	Nicotine x Alcohol	0.005 *	0.002	2.264
Lifetime Drug Use	Alcohol	-0.030	0.042	-0.702
	Cigarette	1.316	1.073	1.227
	E-cigarette	-0.061	0.071	-0.858
	Cigar	0.168 *	0.075	2.232
	Hookah	-0.065	0.053	-1.221
	Chew (smokeless tobacco)	-0.016	0.088	-0.180
	Pipes	0.010	0.054	0.178
	Edible(marijuana in food)	0.004	0.181	0.020
	Inhalant	0.107	0.159	0.671
	Pills of prescription pain relievers	-0.062	0.158	-0.394
	Age	0.000	0.000	-0.221
Sex	Female	0.001	0.005	0.245
Race	Black	0.007	0.009	0.784
	Hispanic	-0.009	0.007	-1.218
	Asian	0.002	0.018	0.117
	Other	-0.015 *	0.008	-1.965
Parental Education	3th grade	0.008	0.193	0.041
	4th grade	0.059	0.194	0.303
	6th grade	0.083	0.163	0.510
	7th grade	0.187	0.182	1.025
	8th grade	0.110	0.164	0.672
	9th grade	0.109	0.160	0.683
	10th grade	0.158	0.160	0.984
	11th grade	0.130	0.159	0.814
	12th grade	0.112	0.160	0.705
	High school graduate	0.127	0.158	0.804
	GED or dquivalend Diploma	0.144	0.159	0.906
	Some college	0.116	0.158	0.734
	Associate degree: Occupational	0.126	0.158	0.799
	Associate degree: Academic Program	0.115	0.158	0.729
	Bachelor's degree	0.118	0.158	0.746
	Master's degree	0.108	0.158	0.685
	Professional School degree	0.112	0.159	0.710
	Doctoral degree	0.123	0.158	0.779
Household Income	$5,000 - $11,999	-0.061 **	0.019	-3.196
	$12,000 - $15,999	-0.005	0.020	-0.261
	$16,000 - $24,999	-0.041 *	0.018	-2.255
	$25,000 - 34,999	-0.005	0.017	-0.307
	$35,000 - $49,999	-0.023	0.017	-1.349
	$50,000 - $74,999	-0.018	0.017	-1.084
	$75,000 - 99,999	-0.010	0.017	-0.602
	$100,000- $199,999	-0.015	0.017	-0.925
	$200,000 and greater	-0.017	0.018	-0.933
Parent Marriage	Widowed	-0.036	0.029	-1.230
	Divorced	0.010	0.008	1.190
	Separated	-0.005	0.013	-0.387
	Never married	0.025 *	0.010	2.516
	Living with partner	0.009	0.011	0.781
Research Site	site 3	0.010	0.013	0.809
	site 4	0.001	0.014	0.064
	site 5	-0.019	0.014	-1.379
	site 6	-0.013	0.012	-1.086
	site 7	-0.013	0.015	-0.881
	site 8	0.007	0.017	0.430
	site 9	-0.027 *	0.013	-2.014
	site 10	0.017	0.013	1.320
	site 11	-0.022	0.014	-1.555
	site 12	-0.018	0.012	-1.419
	site 13	-0.011	0.013	-0.856
	site 14	-0.002	0.012	-0.153
	site 15	-0.017	0.015	-1.069
	site 16	0.001	0.010	0.063
	site 18	-0.018	0.015	-1.174
	site 20	-0.014	0.012	-1.229
	site 21	-0.006	0.012	-0.501
	site 22	0.011	0.037	0.291
	sMRI volume	0.005	0.003	1.711

*** p < .001, ** p < .01, * p < .05

Figure A.6: The results of the polysubstance analysis. The brain activation during correct stop vs correct go in SST and its relationship with regression variables.

Left table header: SST correct stop vs correct go, left pars opercularis — N = 5335

		Coefficient	SE	t-value
	(Intercept)	0.030	0.165	0.181
Prenatal	Nicotine	0.005 *	0.002	2.173
Prenatal	Alcohol	-0.005	0.003	-1.775
Prenatal	Nicotine x Alcohol	0.002	0.002	0.906
Lifetime Drug Use	Alcohol	-0.076	0.043	-1.784
Lifetime Drug Use	Cigarette	0.319	1.087	0.294
Lifetime Drug Use	E-cigarette	-0.006	0.072	-0.085
Lifetime Drug Use	Cigar	0.222 **	0.076	2.913
Lifetime Drug Use	Hookah	-0.045	0.054	-0.845
Lifetime Drug Use	Chew (smokeless tobacco)	0.127	0.089	1.416
Lifetime Drug Use	Pipes	-0.046	0.055	-0.847
Lifetime Drug Use	Edible(marijuana in food)	-0.230	0.184	-1.251
Lifetime Drug Use	Inhalant	0.325 *	0.161	2.013
Lifetime Drug Use	Pills of prescription pain relievers	-0.115	0.160	-0.720
	Age	0.000	0.000	-0.464
Sex	Female	-0.006	0.005	-1.107
Race	Black	0.014	0.009	1.539
Race	Hispanic	-0.004	0.007	-0.609
Race	Asian	0.012	0.018	0.647
Race	Other	-0.019 *	0.008	-2.402
Parental Education	3th grade	-0.020	0.196	-0.105
Parental Education	4th grade	-0.010	0.196	-0.050
Parental Education	6th grade	0.068	0.165	0.411
Parental Education	7th grade	0.153	0.185	0.830
Parental Education	8th grade	0.102	0.166	0.616
Parental Education	9th grade	0.092	0.162	0.569
Parental Education	10th grade	0.061	0.162	0.376
Parental Education	11th grade	0.083	0.161	0.513
Parental Education	12th grade	0.083	0.162	0.511
Parental Education	High school graduate	0.082	0.160	0.510
Parental Education	GED or dquivalend Diploma	0.074	0.161	0.458
Parental Education	Some college	0.065	0.160	0.404
Parental Education	Associate degree: Occupational	0.076	0.160	0.473
Parental Education	Associate degree: Academic Program	0.064	0.160	0.402
Parental Education	Bachelor's degree	0.070	0.160	0.435
Parental Education	Master's degree	0.066	0.160	0.411
Parental Education	Professional School degree	0.060	0.161	0.376
Parental Education	Doctoral degree	0.084	0.160	0.525
Household Income	$5,000 - $11,999	-0.045 *	0.019	-2.318
Household Income	$12,000 - $15,999	-0.029	0.021	-1.392
Household Income	$16,000 - $24,999	-0.034	0.018	-1.841
Household Income	$25,000 - 34,999	-0.006	0.017	-0.353
Household Income	$35,000 - $49,999	-0.025	0.017	-1.461
Household Income	$50,000 - $74,999	-0.014	0.017	-0.810
Household Income	$75,000 - 99,999	-0.004	0.017	-0.230
Household Income	$100,000- $199,999	-0.021	0.017	-1.258
Household Income	$200,000 and greater	-0.016	0.018	-0.897
Parent Marriage	Widowed	-0.035	0.029	-1.209
Parent Marriage	Divorced	0.012	0.008	1.396
Parent Marriage	Separated	-0.015	0.013	-1.148
Parent Marriage	Never married	0.026 *	0.010	2.562
Parent Marriage	Living with partner	0.009	0.012	0.781
Research Site	site 3	0.010	0.013	0.817
Research Site	site 4	0.013	0.014	0.968
Research Site	site 5	-0.019	0.014	-1.350
Research Site	site 6	0.001	0.012	0.104
Research Site	site 7	-0.012	0.015	-0.809
Research Site	site 8	-0.004	0.017	-0.229
Research Site	site 9	-0.009	0.014	-0.637
Research Site	site 10	-0.006	0.013	-0.479
Research Site	site 11	-0.022	0.015	-1.535
Research Site	site 12	-0.015	0.013	-1.209
Research Site	site 13	-0.007	0.013	-0.566
Research Site	site 14	-0.008	0.012	-0.654
Research Site	site 15	-0.016	0.016	-1.027
Research Site	site 16	0.003	0.010	0.306
Research Site	site 18	-0.012	0.015	-0.784
Research Site	site 20	0.009	0.012	0.759
Research Site	site 21	0.007	0.012	0.539
Research Site	site 22	-0.001	0.038	-0.019
	sMRI volume	0.001	0.003	0.292

*** p < .001, ** p < .01, * p < .05

Right table header: SST correct stop vs correct go, right pars opercularis — N = 5336

		Coefficient	SE	t-value
	(Intercept)	0.034	0.172	0.196
Prenatal	Nicotine	0.004	0.002	1.675
Prenatal	Alcohol	-0.007 *	0.003	-2.234
Prenatal	Nicotine x Alcohol	0.003 ***	0.001	4.006
Lifetime Drug Use	Alcohol	-0.051	0.045	-1.142
Lifetime Drug Use	Cigarette	1.046	1.133	0.923
Lifetime Drug Use	E-cigarette	-0.056	0.075	-0.755
Lifetime Drug Use	Cigar	0.140	0.079	1.764
Lifetime Drug Use	Hookah	0.004	0.056	0.072
Lifetime Drug Use	Chew (smokeless tobacco)	0.161	0.093	1.725
Lifetime Drug Use	Pipes	-0.039	0.057	-0.678
Lifetime Drug Use	Edible(marijuana in food)	-0.187	0.192	-0.979
Lifetime Drug Use	Inhalant	0.185	0.168	1.099
Lifetime Drug Use	Pills of prescription pain relievers	-0.086	0.167	-0.515
	Age	0.000	0.000	1.070
Sex	Female	0.008	0.005	1.583
Race	Black	0.001	0.010	0.155
Race	Hispanic	-0.006	0.008	-0.838
Race	Asian	0.018	0.019	0.975
Race	Other	-0.019 *	0.008	-2.380
Parental Education	3th grade	-0.011	0.204	-0.056
Parental Education	4th grade	-0.155	0.205	-0.758
Parental Education	6th grade	0.031	0.172	0.178
Parental Education	7th grade	0.226	0.192	1.174
Parental Education	8th grade	0.104	0.173	0.600
Parental Education	9th grade	0.062	0.169	0.370
Parental Education	10th grade	0.038	0.169	0.226
Parental Education	11th grade	0.050	0.168	0.300
Parental Education	12th grade	0.040	0.168	0.237
Parental Education	High school graduate	0.083	0.167	0.498
Parental Education	GED or dquivalend Diploma	0.061	0.168	0.366
Parental Education	Some college	0.067	0.167	0.402
Parental Education	Associate degree: Occupational	0.081	0.167	0.483
Parental Education	Associate degree: Academic Program	0.075	0.167	0.451
Parental Education	Bachelor's degree	0.068	0.167	0.407
Parental Education	Master's degree	0.066	0.167	0.397
Parental Education	Professional School degree	0.053	0.167	0.316
Parental Education	Doctoral degree	0.069	0.167	0.411
Household Income	$5,000 - $11,999	-0.043 *	0.020	-2.116
Household Income	$12,000 - $15,999	-0.033	0.021	-1.519
Household Income	$16,000 - $24,999	-0.036	0.019	-1.888
Household Income	$25,000 - 34,999	-0.023	0.018	-1.286
Household Income	$35,000 - $49,999	-0.040 *	0.018	-2.264
Household Income	$50,000 - $74,999	-0.023	0.017	-1.339
Household Income	$75,000 - 99,999	-0.017	0.018	-0.951
Household Income	$100,000- $199,999	-0.033	0.018	-1.891
Household Income	$200,000 and greater	-0.025	0.019	-1.325
Parent Marriage	Widowed	-0.048	0.031	-1.555
Parent Marriage	Divorced	0.012	0.009	1.401
Parent Marriage	Separated	-0.019	0.013	-1.469
Parent Marriage	Never married	0.028 **	0.011	2.650
Parent Marriage	Living with partner	0.001	0.012	0.091
Research Site	site 3	-0.001	0.013	-0.039
Research Site	site 4	-0.014	0.014	-0.957
Research Site	site 5	-0.012	0.015	-0.828
Research Site	site 6	-0.010	0.013	-0.791
Research Site	site 7	-0.020	0.016	-1.299
Research Site	site 8	0.009	0.018	0.519
Research Site	site 9	-0.019	0.014	-1.330
Research Site	site 10	-0.013	0.014	-0.965
Research Site	site 11	-0.029	0.015	-1.893
Research Site	site 12	-0.023	0.013	-1.711
Research Site	site 13	-0.044 **	0.013	-3.287
Research Site	site 14	-0.011	0.012	-0.872
Research Site	site 15	-0.030	0.016	-1.826
Research Site	site 16	-0.001	0.011	-0.122
Research Site	site 18	-0.038 *	0.016	-2.396
Research Site	site 20	-0.023	0.012	-1.914
Research Site	site 21	0.001	0.013	0.046
Research Site	site 22	-0.059	0.039	-1.493
	sMRI volume	0.002	0.003	0.782

*** p < .001, ** p < .01, * p < .05

Figure A.7: The results of the polysubstance analysis. The brain activation during correct stop vs correct go in SST and its relationship with regression variables.

SST correct stop vs correct go, right pars triagularis | N = 5336

Group		Coefficient	SE	t-value
	(Intercept)	-0.084	0.235	-0.358
Prenatal	Nicotine	0.007 *	0.003	2.293
	Alcohol	-0.007	0.004	-1.683
	Nicotine x Alcohol	0.003	0.003	1.008
Lifetime Drug Use	Alcohol	-0.037	0.061	-0.603
	Cigarette	0.178	0.239	0.746
	E-cigarette	0.000	0.005	-0.045
	Cigar	0.125	0.108	1.158
	Hookah	-0.009	0.077	-0.118
	Chew (smokeless tobacco)	-0.052	0.127	-0.411
	Pipes	0.019	0.078	0.244
	Edible(marijuana in food)	0.095	0.261	0.365
	Inhalant	0.222	0.230	0.969
	Pills of prescription pain relievers	-0.156	0.228	-0.687
	Age	0.001	0.000	1.767
Sex	Female	-0.001	0.007	-0.161
Race	Black	0.007	0.013	0.553
	Hispanic	-0.015	0.010	-1.450
	Asian	0.016	0.025	0.620
	Other	-0.020	0.011	-1.749
Parental Education	3th grade	-0.057	0.279	-0.206
	4th grade	-0.041	0.280	-0.146
	6th grade	0.021	0.235	0.091
	7th grade	0.098	0.263	0.374
	8th grade	0.123	0.236	0.522
	9th grade	0.066	0.231	0.286
	10th grade	0.064	0.231	0.277
	11th grade	0.042	0.230	0.185
	12th grade	0.034	0.230	0.149
	High school graduate	0.096	0.228	0.419
	GED or dquivalend Diploma	0.107	0.229	0.469
	Some college	0.076	0.228	0.335
	Associate degree: Occupational	0.092	0.228	0.405
	Associate degree: Academic Program	0.072	0.228	0.317
	Bachelor's degree	0.081	0.228	0.354
	Master's degree	0.077	0.228	0.338
	Professional School degree	0.069	0.229	0.302
	Doctoral degree	0.064	0.229	0.279
Household Income	$5,000 - $11,999	-0.065 *	0.028	-2.334
	$12,000 - $15,999	0.000	0.029	-0.014
	$16,000 - $24,999	-0.027	0.026	-1.017
	$25,000 - 34,999	-0.024	0.025	-0.958
	$35,000 - $49,999	-0.017	0.024	-0.699
	$50,000 - $74,999	-0.009	0.024	-0.398
	$75,000 - 99,999	0.001	0.024	0.051
	$100,000- $199,999	-0.013	0.024	-0.533
	$200,000 and greater	0.005	0.026	0.180
Parent Marriage	Widowed	-0.031	0.042	-0.750
	Divorced	0.025 *	0.012	2.049
	Separated	-0.005	0.018	-0.257
	Never married	0.034 *	0.014	2.390
	Living with partner	0.017	0.017	1.018
Research Site	site 3	0.025	0.018	1.410
	site 4	0.017	0.019	0.895
	site 5	-0.014	0.020	-0.678
	site 6	-0.013	0.017	-0.781
	site 7	-0.030	0.021	-1.413
	site 8	0.046	0.024	1.886
	site 9	-0.031	0.019	-1.604
	site 10	0.012	0.019	0.641
	site 11	-0.019	0.021	-0.918
	site 12	-0.048 **	0.018	-2.690
	site 13	-0.017	0.018	-0.936
	site 14	-0.014	0.017	-0.855
	site 15	-0.054 *	0.022	-2.428
	site 16	0.006	0.015	0.402
	site 18	-0.012	0.022	-0.530
	site 20	-0.021	0.017	-1.268
	site 21	0.005	0.018	0.290
	site 22	-0.008	0.054	-0.152
	sMRI volume	0.008	0.004	1.885

*** p < .001, ** p < .01, * p < .05

SST correct stop vs correct go, left pars triangularis | N = 5336

Group		Coefficient	SE	t-value
	(Intercept)	-0.040	0.235	-0.170
Prenatal	Nicotine	0.008 *	0.003	2.507
	Alcohol	-0.006	0.004	-1.505
	Nicotine x Alcohol	0.003	0.003	0.953
Lifetime Drug Use	Alcohol	-0.033	0.061	-0.545
	Cigarette	0.161	0.240	0.671
	E-cigarette	-0.001	0.005	-0.149
	Cigar	0.221 *	0.108	2.043
	Hookah	-0.062	0.077	-0.810
	Chew (smokeless tobacco)	0.032	0.127	0.249
	Pipes	-0.037	0.078	-0.480
	Edible(marijuana in food)	-0.469	0.262	-1.792
	Inhalant	0.203	0.230	0.881
	Pills of prescription pain relievers	-0.177	0.228	-0.778
	Age	0.000	0.000	0.010
Sex	Female	-0.016 *	0.007	-2.230
Race	Black	0.031 *	0.013	2.362
	Hispanic	-0.001	0.010	-0.055
	Asian	0.014	0.026	0.550
	Other	-0.026 *	0.011	-2.320
Parental Education	3th grade	-0.002	0.279	-0.009
	4th grade	0.076	0.280	0.270
	6th grade	0.043	0.235	0.182
	7th grade	0.080	0.263	0.305
	8th grade	0.111	0.236	0.470
	9th grade	0.052	0.231	0.224
	10th grade	0.105	0.231	0.457
	11th grade	0.076	0.230	0.331
	12th grade	0.051	0.230	0.223
	High school graduate	0.081	0.228	0.357
	GED or dquivalend Diploma	0.092	0.229	0.402
	Some college	0.062	0.228	0.272
	Associate degree: Occupational	0.078	0.228	0.343
	Associate degree: Academic Program	0.066	0.228	0.287
	Bachelor's degree	0.064	0.228	0.281
	Master's degree	0.067	0.228	0.293
	Professional School degree	0.068	0.229	0.299
	Doctoral degree	0.067	0.229	0.294
Household Income	$5,000 - $11,999	-0.080 **	0.028	-2.888
	$12,000 - $15,999	-0.006	0.029	-0.195
	$16,000 - $24,999	-0.024	0.026	-0.897
	$25,000 - 34,999	-0.005	0.025	-0.214
	$35,000 - $49,999	-0.022	0.024	-0.901
	$50,000 - $74,999	-0.003	0.024	-0.109
	$75,000 - 99,999	0.012	0.024	0.515
	$100,000- $199,999	-0.003	0.024	-0.119
	$200,000 and greater	-0.005	0.026	-0.210
Parent Marriage	Widowed	-0.028	0.042	-0.668
	Divorced	0.036 **	0.012	3.001
	Separated	-0.004	0.018	-0.204
	Never married	0.039 **	0.014	2.730
	Living with partner	0.014	0.017	0.867
Research Site	site 3	0.019	0.018	1.062
	site 4	0.042 *	0.019	2.163
	site 5	-0.019	0.020	-0.946
	site 6	-0.006	0.017	-0.376
	site 7	-0.020	0.021	-0.925
	site 8	0.045	0.024	1.864
	site 9	-0.036	0.019	-1.881
	site 10	0.022	0.019	1.159
	site 11	-0.010	0.021	-0.460
	site 12	-0.038 *	0.018	-2.105
	site 13	0.018	0.018	0.996
	site 14	0.003	0.017	0.179
	site 15	-0.040	0.022	-1.787
	site 16	0.004	0.015	0.264
	site 18	0.016	0.022	0.716
	site 20	0.030	0.017	1.767
	site 21	0.005	0.018	0.274
	site 22	0.033	0.054	0.619
	sMRI volume	0.009 *	0.004	2.064

*** p < .001, ** p < .01, * p < .05

Figure A.8: The results of the polysubstance analysis. The brain activation during correct stop vs correct go in SST and its relationship with regression variables.

SST correct stop vs correct go, left pars orbitarlis				N = 5336
		Coefficient	SE	t-value
	(Intercept)	-0.045	0.633	-0.071
Prenatal	Nicotine	0.000	0.009	0.030
	Alcohol	0.008	0.011	0.728
	Nicotine x Alcohol	0.009 ***	0.003	3.398
Lifetime Drug Use	Alcohol	-0.001	0.164	-0.007
	Cigarette	0.017	0.102	0.166
	E-cigarette	0.000	0.013	-0.034
	Cigar	0.200	0.292	0.684
	Hookah	-0.165	0.207	-0.799
	Chew (smokeless tobacco)	-0.053	0.344	-0.155
	Pipes	0.058	0.210	0.276
	Edible(marijuana in food)	-0.102	0.706	-0.145
	Inhalant	0.154	0.620	0.248
	Pills of prescription pain relievers	-0.002	0.614	-0.003
	Age	0.000	0.001	-0.262
Sex	Female	-0.024	0.019	-1.253
Race	Black	-0.030	0.036	-0.847
	Hispanic	-0.056 *	0.028	-1.984
	Asian	-0.003	0.069	-0.046
	Other	-0.057	0.030	-1.903
Parental Education	3th grade	-0.053	0.753	-0.071
	4th grade	0.223	0.755	0.295
	6th grade	0.039	0.635	0.061
	7th grade	-0.021	0.709	-0.029
	8th grade	0.067	0.638	0.105
	9th grade	0.143	0.622	0.230
	10th grade	0.220	0.623	0.352
	11th grade	0.212	0.621	0.341
	12th grade	0.131	0.621	0.211
	High school graduate	0.119	0.616	0.193
	GED or dquivalend Diploma	0.144	0.618	0.233
	Some college	0.066	0.615	0.107
	Associate degree: Occupational	0.088	0.616	0.143
	Associate degree: Academic Program	0.046	0.616	0.075
	Bachelor's degree	0.054	0.615	0.087
	Master's degree	0.054	0.615	0.088
	Professional School degree	0.032	0.617	0.051
	Doctoral degree	0.014	0.617	0.023
Household Income	$5,000 - $11,999	-0.175 *	0.075	-2.347
	$12,000 - $15,999	-0.007	0.079	-0.086
	$16,000 - $24,999	-0.035	0.071	-0.495
	$25,000 - 34,999	0.052	0.067	0.779
	$35,000 - $49,999	-0.026	0.065	-0.406
	$50,000 - $74,999	0.000	0.064	0.005
	$75,000 - 99,999	0.032	0.065	0.488
	$100,000- $199,999	0.029	0.065	0.439
	$200,000 and greater	0.057	0.069	0.833
Parent Marriage	Widowed	-0.020	0.113	-0.181
	Divorced	0.061	0.032	1.889
	Separated	-0.018	0.049	-0.372
	Never married	0.065	0.039	1.664
	Living with partner	0.069	0.045	1.558
Research Site	site 3	0.064	0.049	1.309
	site 4	0.117 *	0.053	2.234
	site 5	-0.039	0.054	-0.727
	site 6	-0.014	0.046	-0.307
	site 7	-0.056	0.058	-0.963
	site 8	0.075	0.066	1.136
	site 9	-0.067	0.052	-1.288
	site 10	0.084	0.051	1.643
	site 11	-0.008	0.056	-0.139
	site 12	-0.113 *	0.048	-2.340
	site 13	0.030	0.049	0.608
	site 14	0.006	0.045	0.123
	site 15	-0.029	0.060	-0.475
	site 16	-0.008	0.040	-0.191
	site 18	-0.024	0.059	-0.411
	site 20	-0.013	0.045	-0.286
	site 21	0.026	0.048	0.555
	site 22	0.102	0.145	0.702
	sMRI volume	0.000	0.011	-0.012

*** p < .001, ** p < .01, * p < .05

Figure A.9: The results of the polysubstance analysis. The brain activation during correct stop vs correct go in SST and its relationship with regression variables.

67

SST correct stop vs incorrect stop, left pars opercularis — N = 5337

		Coefficient	SE	t-value
	(Intercept)	0.124	0.190	0.653
Prenatal	Nicotine	0.002	0.003	0.788
	Alcohol	-0.005	0.003	-1.658
	Nicotine x Alcohol	0.004 ***	0.001	5.728
Lifetime Drug Use	Alcohol	-0.052	0.049	-1.047
	Cigarette	-0.017	0.030	-0.555
	E-cigarette	0.000	0.004	0.073
	Cigar	-0.164	0.218	-0.756
	Hookah	-0.047	0.062	-0.756
	Chew (smokeless tobacco)	0.167	0.118	1.407
	Pipes	-0.098	0.065	-1.508
	Edible(marijuana in food)	-0.295	0.219	-1.345
	Inhalant	0.024	0.186	0.129
	Pills of prescription pain relievers	-0.019	0.184	-0.103
Age	Age	0.000	0.000	-0.079
Sex	Female	-0.007	0.006	-1.164
Race	Black	0.002	0.011	0.177
	Hispanic	-0.008	0.008	-0.945
	Asian	0.026	0.021	1.268
	Other	-0.021 *	0.009	-2.307
Parental Education	3th grade	-0.280	0.225	-1.242
	4th grade	-0.097	0.226	-0.430
	6th grade	-0.144	0.190	-0.756
	7th grade	-0.233	0.212	-1.096
	8th grade	-0.142	0.191	-0.746
	9th grade	-0.103	0.186	-0.550
	10th grade	-0.129	0.187	-0.692
	11th grade	-0.131	0.186	-0.705
	12th grade	-0.081	0.186	-0.436
	High school graduate	-0.124	0.184	-0.671
	GED or dquivalend Diploma	-0.125	0.185	-0.674
	Some college	-0.141	0.184	-0.764
	Associate degree: Occupational	-0.130	0.184	-0.707
	Associate degree: Academic Program	-0.115	0.185	-0.622
	Bachelor's degree	-0.130	0.184	-0.703
	Master's degree	-0.138	0.184	-0.748
	Professional School degree	-0.130	0.185	-0.702
	Doctoral degree	-0.133	0.185	-0.718
Household Income	$5,000 - $11,999	-0.041	0.022	-1.833
	$12,000 - $15,999	-0.012	0.024	-0.522
	$16,000 - $24,999	-0.052 *	0.021	-2.467
	$25,000 - 34,999	-0.004	0.020	-0.201
	$35,000 - $49,999	-0.005	0.019	-0.242
	$50,000 - $74,999	-0.009	0.019	-0.477
	$75,000 - 99,999	-0.007	0.020	-0.346
	$100,000- $199,999	-0.015	0.019	-0.768
	$200,000 and greater	-0.012	0.021	-0.585
Parent Marriage	Widowed	-0.037	0.034	-1.104
	Divorced	0.005	0.010	0.547
	Separated	-0.020	0.015	-1.388
	Never married	0.023 *	0.012	1.986
	Living with partner	0.021	0.013	1.572
Research Site	site 3	0.017	0.015	1.136
	site 4	0.033 *	0.016	2.108
	site 5	-0.001	0.016	-0.041
	site 6	0.003	0.014	0.250
	site 7	0.014	0.017	0.792
	site 8	-0.007	0.020	-0.366
	site 9	-0.008	0.016	-0.491
	site 10	0.015	0.015	0.995
	site 11	-0.002	0.017	-0.090
	site 12	-0.003	0.015	-0.230
	site 13	0.006	0.015	0.429
	site 14	0.018	0.014	1.359
	site 15	0.013	0.018	0.700
	site 16	0.005	0.012	0.398
	site 18	0.027	0.018	1.523
	site 20	0.006	0.013	0.439
	site 21	0.003	0.014	0.238
	site 22	0.045	0.044	1.045
sMRI volume		0.003	0.003	0.913

*** p < .001, ** p < .01, * p < .05

SST correct stop vs incorrect stop, right caudal ACC — N = 5337

		Coefficient	SE	t-value
	(Intercept)	0.006	0.193	0.029
Prenatal	Nicotine	-0.002	0.003	-0.708
	Alcohol	-0.001	0.003	-0.277
	Nicotine x Alcohol	0.003 ***	0.001	3.669
Lifetime Drug Use	Alcohol	-0.036	0.050	-0.713
	Cigarette	0.012	0.031	0.372
	E-cigarette	0.000	0.004	0.073
	Cigar	-0.199	0.222	-0.899
	Hookah	-0.025	0.063	-0.399
	Chew (smokeless tobacco)	0.087	0.121	0.723
	Pipes	-0.041	0.066	-0.625
	Edible(marijuana in food)	-0.200	0.224	-0.896
	Inhalant	-0.036	0.189	-0.188
	Pills of prescription pain relievers	0.000	0.188	0.000
Age	Age	0.000	0.000	0.396
Sex	Female	-0.010	0.006	-1.644
Race	Black	0.008	0.011	0.714
	Hispanic	-0.011	0.009	-1.265
	Asian	0.003	0.021	0.167
	Other	-0.017	0.009	-1.853
Parental Education	3th grade	-0.255	0.230	-1.107
	4th grade	0.105	0.231	0.455
	6th grade	-0.064	0.194	-0.332
	7th grade	-0.112	0.217	-0.517
	8th grade	-0.065	0.195	-0.334
	9th grade	-0.007	0.190	-0.036
	10th grade	-0.001	0.190	-0.007
	11th grade	-0.036	0.190	-0.187
	12th grade	-0.018	0.190	-0.097
	High school graduate	-0.028	0.188	-0.152
	GED or dquivalend Diploma	0.000	0.189	0.000
	Some college	-0.024	0.188	-0.126
	Associate degree: Occupational	-0.013	0.188	-0.068
	Associate degree: Academic Program	-0.014	0.188	-0.074
	Bachelor's degree	-0.018	0.188	-0.096
	Master's degree	-0.039	0.188	-0.206
	Professional School degree	-0.026	0.188	-0.138
	Doctoral degree	-0.044	0.188	-0.231
Household Income	$5,000 - $11,999	-0.023	0.023	-1.005
	$12,000 - $15,999	0.012	0.024	0.481
	$16,000 - $24,999	-0.028	0.022	-1.316
	$25,000 - 34,999	0.004	0.020	0.184
	$35,000 - $49,999	0.020	0.020	1.003
	$50,000 - $74,999	0.007	0.020	0.332
	$75,000 - 99,999	0.006	0.020	0.326
	$100,000- $199,999	0.007	0.020	0.329
	$200,000 and greater	0.007	0.021	0.330
Parent Marriage	Widowed	-0.062	0.034	-1.808
	Divorced	0.002	0.010	0.214
	Separated	-0.010	0.015	-0.651
	Never married	0.004	0.012	0.355
	Living with partner	0.002	0.014	0.180
Research Site	site 3	0.008	0.015	0.516
	site 4	0.011	0.016	0.696
	site 5	-0.022	0.016	-1.347
	site 6	-0.006	0.014	-0.431
	site 7	0.003	0.018	0.178
	site 8	-0.035	0.020	-1.748
	site 9	-0.035 *	0.016	-2.177
	site 10	0.010	0.016	0.640
	site 11	-0.005	0.017	-0.292
	site 12	-0.020	0.015	-1.335
	site 13	-0.002	0.015	-0.125
	site 14	0.015	0.014	1.104
	site 15	0.006	0.018	0.301
	site 16	-0.006	0.012	-0.499
	site 18	-0.003	0.018	-0.157
	site 20	-0.012	0.014	-0.839
	site 21	0.005	0.015	0.354
	site 22	0.057	0.044	1.292
sMRI volume		0.000	0.003	0.011

*** p < .001, ** p < .01, * p < .05

Figure A.10: The results of the polysubstance analysis. The brain activation during correct stop vs incorrect stop in SST and its relationship with regression variables.

SST correct stop vs incorrect stop, left pars opercularis   N = 5337

		Coefficient	SE	t-value
	(Intercept)	0.124	0.190	0.653
Prenatal	Nicotine	0.002	0.003	0.788
	Alcohol	-0.005	0.003	-1.658
	Nicotine x Alcohol	0.004 ***	0.001	5.728
Lifetime Drug Use	Alcohol	-0.052	0.049	-1.047
	Cigarette	-0.017	0.030	-0.555
	E-cigarette	0.000	0.004	0.073
	Cigar	-0.164	0.218	-0.756
	Hookah	-0.047	0.062	-0.756
	Chew (smokeless tobacco)	0.167	0.118	1.407
	Pipes	-0.098	0.065	-1.508
	Edible(marijuana in food)	-0.295	0.219	-1.345
	Inhalant	0.024	0.186	0.129
	Pills of prescription pain relievers	-0.019	0.184	-0.103
	Age	0.000	0.000	-0.079
Sex	Female	-0.007	0.006	-1.164
Race	Black	0.002	0.011	0.177
	Hispanic	-0.008	0.008	-0.945
	Asian	0.026	0.021	1.268
	Other	-0.021 *	0.009	-2.307
Parental Education	3th grade	-0.280	0.225	-1.242
	4th grade	-0.097	0.226	-0.430
	6th grade	-0.144	0.190	-0.756
	7th grade	-0.233	0.212	-1.096
	8th grade	-0.142	0.191	-0.746
	9th grade	-0.103	0.186	-0.550
	10th grade	-0.129	0.187	-0.692
	11th grade	-0.131	0.186	-0.705
	12th grade	-0.081	0.186	-0.436
	High school graduate	-0.124	0.184	-0.671
	GED or dquivalend Diploma	-0.125	0.185	-0.674
	Some college	-0.141	0.184	-0.764
	Associate degree: Occupational	-0.130	0.184	-0.707
	Associate degree: Academic Program	-0.115	0.185	-0.622
	Bachelor's degree	-0.130	0.184	-0.703
	Master's degree	-0.138	0.184	-0.748
	Professional School degree	-0.130	0.185	-0.702
	Doctoral degree	-0.133	0.185	-0.718
Household Income	$5,000 - $11,999	-0.041	0.022	-1.833
	$12,000 - $15,999	-0.012	0.024	-0.522
	$16,000 - $24,999	-0.052 *	0.021	-2.467
	$25,000 - 34,999	-0.004	0.020	-0.201
	$35,000 - $49,999	-0.005	0.019	-0.242
	$50,000 - $74,999	-0.009	0.019	-0.477
	$75,000 - 99,999	-0.007	0.020	-0.346
	$100,000- $199,999	-0.015	0.019	-0.768
	$200,000 and greater	-0.012	0.021	-0.585
Parent Marriage	Widowed	-0.037	0.034	-1.104
	Divorced	0.005	0.010	0.547
	Separated	-0.020	0.015	-1.388
	Never married	0.023 *	0.012	1.986
	Living with partner	0.021	0.013	1.572
Research Site	site 3	0.017	0.015	1.136
	site 4	0.033 *	0.016	2.108
	site 5	-0.001	0.016	-0.041
	site 6	0.003	0.014	0.250
	site 7	0.014	0.017	0.792
	site 8	-0.007	0.020	-0.366
	site 9	-0.008	0.016	-0.491
	site 10	0.015	0.015	0.995
	site 11	-0.002	0.017	-0.090
	site 12	-0.003	0.015	-0.230
	site 13	0.006	0.015	0.429
	site 14	0.018	0.014	1.359
	site 15	0.013	0.018	0.700
	site 16	0.005	0.012	0.398
	site 18	0.027	0.018	1.523
	site 20	0.006	0.013	0.439
	site 21	0.003	0.014	0.238
	site 22	0.045	0.044	1.045
	sMRI volume	0.003	0.003	0.913

*** p < .001, ** p < .01, * p < .05

SST correct stop vs incorrect stop, right caudal ACC   N = 5337

		Coefficient	SE	t-value
	(Intercept)	0.006	0.193	0.029
Prenatal	Nicotine	-0.002	0.003	-0.708
	Alcohol	-0.001	0.003	-0.277
	Nicotine x Alcohol	0.003 ***	0.001	3.669
Lifetime Drug Use	Alcohol	-0.036	0.050	-0.713
	Cigarette	0.012	0.031	0.372
	E-cigarette	0.000	0.004	0.073
	Cigar	-0.199	0.222	-0.899
	Hookah	-0.025	0.063	-0.399
	Chew (smokeless tobacco)	0.087	0.121	0.723
	Pipes	-0.041	0.066	-0.625
	Edible(marijuana in food)	-0.200	0.224	-0.896
	Inhalant	-0.036	0.189	-0.188
	Pills of prescription pain relievers	0.000	0.188	0.000
	Age	0.000	0.000	0.396
Sex	Female	-0.010	0.006	-1.644
Race	Black	0.008	0.011	0.714
	Hispanic	-0.011	0.009	-1.265
	Asian	0.003	0.021	0.167
	Other	-0.017	0.009	-1.853
Parental Education	3th grade	-0.255	0.230	-1.107
	4th grade	0.105	0.231	0.455
	6th grade	-0.064	0.194	-0.332
	7th grade	-0.112	0.217	-0.517
	8th grade	-0.065	0.195	-0.334
	9th grade	-0.007	0.190	-0.036
	10th grade	-0.001	0.190	-0.007
	11th grade	-0.036	0.190	-0.187
	12th grade	-0.018	0.190	-0.097
	High school graduate	-0.028	0.188	-0.152
	GED or dquivalend Diploma	0.000	0.189	0.000
	Some college	-0.024	0.188	-0.126
	Associate degree: Occupational	-0.013	0.188	-0.068
	Associate degree: Academic Program	-0.014	0.188	-0.074
	Bachelor's degree	-0.018	0.188	-0.096
	Master's degree	-0.039	0.188	-0.206
	Professional School degree	-0.026	0.188	-0.138
	Doctoral degree	-0.044	0.188	-0.231
Household Income	$5,000 - $11,999	-0.023	0.023	-1.005
	$12,000 - $15,999	0.012	0.024	0.481
	$16,000 - $24,999	-0.028	0.022	-1.316
	$25,000 - 34,999	0.004	0.020	0.184
	$35,000 - $49,999	0.020	0.020	1.003
	$50,000 - $74,999	0.007	0.020	0.332
	$75,000 - 99,999	0.006	0.020	0.326
	$100,000- $199,999	0.007	0.020	0.329
	$200,000 and greater	0.007	0.021	0.330
Parent Marriage	Widowed	-0.062	0.034	-1.808
	Divorced	0.002	0.010	0.214
	Separated	-0.010	0.015	-0.651
	Never married	0.004	0.012	0.355
	Living with partner	0.002	0.014	0.180
Research Site	site 3	0.008	0.015	0.516
	site 4	0.011	0.016	0.696
	site 5	-0.022	0.016	-1.347
	site 6	-0.006	0.014	-0.431
	site 7	0.003	0.018	0.178
	site 8	-0.035	0.020	-1.748
	site 9	-0.035 *	0.016	-2.177
	site 10	0.010	0.016	0.640
	site 11	-0.005	0.017	-0.292
	site 12	-0.020	0.015	-1.335
	site 13	-0.002	0.015	-0.125
	site 14	0.015	0.014	1.104
	site 15	0.006	0.018	0.301
	site 16	-0.006	0.012	-0.499
	site 18	-0.003	0.018	-0.157
	site 20	-0.012	0.014	-0.839
	site 21	0.005	0.015	0.354
	site 22	0.057	0.044	1.292
	sMRI volume	0.000	0.003	0.011

*** p < .001, ** p < .01, * p < .05

Figure A.11: The results of the polysubstance analysis. The brain activation during correct stop vs incorrect stop in SST and its relationship with regression variables.
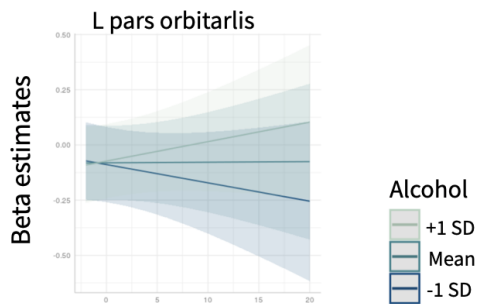
SST correct stop vs incorrect stop, left caudal ACC				N = 5337
		Coefficient	SE	t-value
	(Intercept)	0.015	0.194	0.077
Prenatal	Nicotine	-0.001	0.003	-0.498
	Alcohol	-0.002	0.003	-0.564
	Nicotine x Alcohol	0.004 ***	0.001	4.919
Lifetime Drug Use	Alcohol	0.004	0.050	0.071
	Cigarette	0.107	0.198	0.540
	E-cigarette	-0.001	0.004	-0.142
	Cigar	-0.281	0.222	-1.266
	Hookah	0.003	0.063	0.051
	Chew (smokeless tobacco)	0.189	0.121	1.568
	Pipes	-0.066	0.066	-1.002
	Edible(marijuana in food)	-0.033	0.224	-0.148
	Inhalant	-0.010	0.189	-0.053
	Pills of prescription pain relievers	0.035	0.188	0.185
	Age	0.000	0.000	-0.021
Sex	Female	0.001	0.006	0.120
Race	Black	0.006	0.011	0.528
	Hispanic	-0.011	0.009	-1.295
	Asian	0.010	0.021	0.481
	Other	-0.013	0.009	-1.364
Parental Education	3th grade	-0.233	0.230	-1.012
	4th grade	0.040	0.231	0.171
	6th grade	-0.086	0.194	-0.446
	7th grade	-0.027	0.217	-0.127
	8th grade	-0.030	0.195	-0.154
	9th grade	0.010	0.190	0.053
	10th grade	0.002	0.190	0.008
	11th grade	-0.027	0.190	-0.140
	12th grade	-0.012	0.190	-0.064
	High school graduate	-0.020	0.188	-0.105
	GED or dquivalend Diploma	0.011	0.189	0.059
	Some college	-0.027	0.188	-0.146
	Associate degree: Occupational	-0.019	0.188	-0.101
	Associate degree: Academic Program	-0.021	0.188	-0.113
	Bachelor's degree	-0.024	0.188	-0.126
	Master's degree	-0.039	0.188	-0.205
	Professional School degree	-0.026	0.189	-0.140
	Doctoral degree	-0.054	0.189	-0.285
Household Income	$5,000 - $11,999	-0.027	0.023	-1.175
	$12,000 - $15,999	0.009	0.024	0.374
	$16,000 - $24,999	-0.027	0.022	-1.228
	$25,000 - 34,999	0.005	0.020	0.258
	$35,000 - $49,999	0.021	0.020	1.073
	$50,000 - $74,999	0.003	0.020	0.153
	$75,000 - 99,999	0.011	0.020	0.535
	$100,000- $199,999	0.004	0.020	0.179
	$200,000 and greater	0.002	0.021	0.109
Parent Marriage	Widowed	-0.062	0.035	-1.805
	Divorced	-0.008	0.010	-0.852
	Separated	-0.016	0.015	-1.089
	Never married	0.007	0.012	0.620
	Living with partner	0.007	0.014	0.479
Research Site	site 3	0.010	0.015	0.659
	site 4	0.021	0.016	1.282
	site 5	-0.016	0.016	-0.986
	site 6	-0.003	0.014	-0.217
	site 7	0.011	0.018	0.617
	site 8	-0.033	0.020	-1.667
	site 9	-0.019	0.016	-1.169
	site 10	0.007	0.016	0.430
	site 11	-0.003	0.017	-0.203
	site 12	-0.023	0.015	-1.520
	site 13	0.006	0.015	0.387
	site 14	0.024	0.014	1.711
	site 15	0.003	0.018	0.172
	site 16	-0.003	0.012	-0.243
	site 18	0.028	0.018	1.538
	site 20	-0.014	0.014	-1.003
	site 21	0.001	0.015	0.053
	site 22	0.051	0.044	1.147
	sMRI volume	0.002	0.003	0.624

*** p < .001, ** p < .01, * p < .05

Figure A.12: The results of the polysubstance analysis. The brain activation during correct stop vs incorrect stop in SST and its relationship with regression variables.
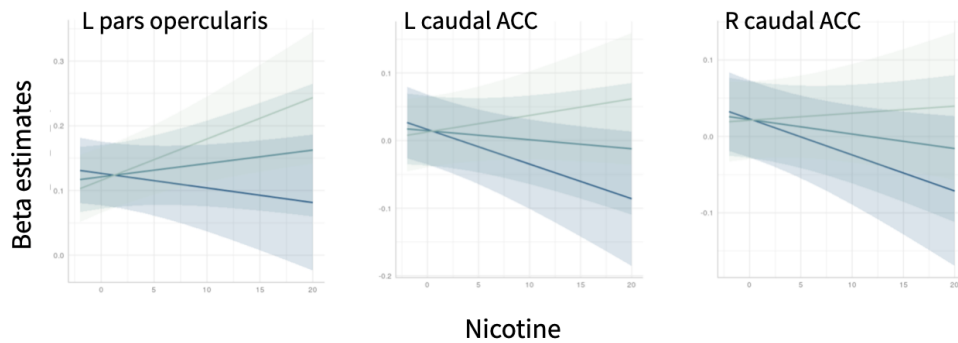
Figure A.13: The results of the polysubstance analysis. The interaction plots of nicotine and alcohol.

UPPS-P total

R squared = 0.008 — N = 724

		Coefficient		SE	t-value
(Intercept)		40.674	***	0.415	97.912
Prenatal	Nicotine	1.566	**	0.587	2.666

*** p < .001, ** p < .01, * p < .05

SST correct stop vs correct go, right pars opercularis — N = 474

		Coefficient		SE	t-value
(Intercept)		0.101	***	0.010	9.761
Prenatal	Nicotine	0.033	*	0.015	2.247

*** p < .001, ** p < .01, * p < .05

UPPS-P total

R squared = 0.002 — N = 3114

		Coefficient		SE	t-value
(Intercept)		40.967	***	0.131	312.190
Prenatal	Nicotine	0.350	**	0.132	2.659
	Alcohol	0.018		0.132	0.134

*** p < .001, ** p < .01, * p < .05

MID reward receipt, rigth accumbens area — N = 2126

		Coefficient		SE	t-value
(Intercept)		0.137	***	0.008	16.349
Prenatal	Nicotine	0.024	**	0.008	2.821
	Alcohol	-0.001		0.008	-0.122

*** p < .001, ** p < .01, * p < .05

SST correct stop vs correct go, left pars triagularis — N = 2126

		Coefficient		SE	t-value
(Intercept)		0.028	***	0.005	5.817
Prenatal	Nicotine	0.015	**	0.005	3.184
	Alcohol	-0.002		0.005	-0.389

*** p < .001, ** p < .01, * p < .05

SST correct stop vs correct go, left pars opercularis — N = 2126

		Coefficient		SE	t-value
(Intercept)		0.060	***	0.003	17.442
Prenatal	Nicotine	0.011	**	0.003	3.178
	Alcohol	-0.003		0.003	-0.977

*** p < .001, ** p < .01, * p < .05

SST correct stop vs correct go, right pars triagularis — N = 2126

		Coefficient		SE	t-value
(Intercept)		0.070	***	0.005	13.517
Prenatal	Nicotine	0.011	*	0.005	2.118
	Alcohol	-0.005		0.005	-1.031

*** p < .001, ** p < .01, * p < .05

SST correct stop vs incorrect stop, left right opercularis — N = 2126

		Coefficient		SE	t-value
(Intercept)		-0.002		0.004	-0.543
Prenatal	Nicotine	0.001		0.004	0.290
	Alcohol	-0.009	*	0.004	-2.055

*** p < .001, ** p < .01, * p < .05

SST correct stop vs incorrect stop, left pars opercularis — N = 2126

		Coefficient		SE	t-value
(Intercept)		-0.021	***	0.004	-5.483
Prenatal	Nicotine	0.004		0.004	1.151
	Alcohol	-0.008	*	0.004	-2.048

*** p < .001, ** p < .01, * p < .05

SST correct stop vs incorrect stop, right pars triangularis — N = 2126

		Coefficient		SE	t-value
(Intercept)		0.009		0.006	1.601
Prenatal	Nicotine	0.012	*	0.006	2.042
	Alcohol	-0.010		0.006	-1.697

*** p < .001, ** p < .01, * p < .05

Figure A.14: The results of propensity score matching analysis.

ELS1, SST correct stop vs correct go, left pars orbitalris — N = 2260

		Coefficient	SE	t-value
	(Intercept)	0.494	0.704	0.702
Prenatal	Nicotine	0.005	0.015	0.353
	Alcohol	0.012	0.020	0.574
	Nicotine x Alcohol	0.013 **	0.005	2.699
Lifetime Drug Use	Alcohol	0.045	0.198	0.227
	Cigarette	0.634	4.416	0.144
	E-cigarette	-0.050	0.291	-0.170
	Cigar	0.228	0.342	0.667
	Hookah	-0.302	0.335	-0.902
	Chew (smokeless tobacco)	-0.244	0.564	-0.433
	Pipes	0.147	0.268	0.547
	Inhalant	0.218	0.659	0.331
	Pills of prescription pain relievers	-0.055	0.648	-0.085
	Age	-0.002	0.002	-0.839
Sex	Female	-0.058	0.032	-1.788
Race	Black	0.058	0.054	1.091
	Hispanic	-0.004	0.044	-0.094
	Asian	0.002	0.131	0.017
	Other	-0.071	0.047	-1.487
Parental Education	6th grade	-0.455	0.713	-0.638
	7th grade	-0.498	0.803	-0.620
	8th grade	-0.591	0.763	-0.775
	9th grade	-0.311	0.679	-0.458
	10th grade	-0.048	0.676	-0.071
	11th grade	-0.365	0.673	-0.542
	12th grade	-0.688	0.675	-1.021
	High school graduate	-0.260	0.663	-0.392
	GED or dquivalend Diploma	-0.324	0.667	-0.485
	Some college	-0.321	0.662	-0.485
	Associate degree: Occupational	-0.327	0.663	-0.493
	Associate degree: Academic Program	-0.423	0.664	-0.637
	Bachelor's degree	-0.355	0.662	-0.536
	Master's degree	-0.324	0.663	-0.489
	Professional School degree	-0.400	0.666	-0.601
	Doctoral degree	-0.325	0.667	-0.487
Household Income	$5,000 - $11,999	-0.208	0.115	-1.809
	$12,000 - $15,999	-0.014	0.123	-0.113
	$16,000 - $24,999	-0.068	0.111	-0.613
	$25,000 - 34,999	0.073	0.103	0.709
	$35,000 - $49,999	0.003	0.101	0.030
	$50,000 - $74,999	0.025	0.101	0.249
	$75,000 - 99,999	0.060	0.103	0.584
	$100,000- $199,999	0.081	0.103	0.782
	$200,000 and greater	0.149	0.113	1.326
Parent Marriage	Widowed	0.019	0.179	0.108
	Divorced	0.041	0.043	0.942
	Separated	0.028	0.066	0.427
	Never married	0.077	0.059	1.303
	Living with partner	0.077	0.071	1.097
Research Site	site 3	0.081	0.081	1.002
	site 4	0.179 *	0.082	2.197
	site 5	-0.127	0.091	-1.390
	site 6	-0.039	0.076	-0.511
	site 7	-0.068	0.094	-0.721
	site 8	-0.088	0.130	-0.678
	site 9	-0.118	0.086	-1.374
	site 10	0.119	0.083	1.432
	site 11	-0.030	0.086	-0.350
	site 12	-0.116	0.082	-1.416
	site 13	-0.015	0.081	-0.179
	site 14	-0.024	0.077	-0.313
	site 15	-0.004	0.091	-0.040
	site 16	-0.041	0.066	-0.622
	site 18	0.026	0.102	0.250
	site 20	0.007	0.074	0.095
	site 21	0.032	0.080	0.406
	site 22	0.110	0.239	0.459
	sMRI volume	-0.013	0.018	-0.719

*** p < .001, ** p < .01, * p < .05

ELS1, SST correct stop vs correct go, left pars triangularis — N = 2260

		Coefficient	SE	t-value
	(Intercept)	-0.069	0.274	-0.251
Prenatal	Nicotine	0.016 **	0.006	2.801
	Alcohol	-0.011	0.008	-1.447
	Nicotine x Alcohol	0.002	0.011	0.149
Lifetime Drug Use	Alcohol	-0.015	0.077	-0.188
	Cigarette	0.561	1.721	0.326
	E-cigarette	-0.027	0.114	-0.234
	Cigar	0.229	0.133	1.721
	Hookah	-0.116	0.130	-0.893
	Chew (smokeless tobacco)	-0.016	0.220	-0.074
	Pipes	-0.013	0.104	-0.121
	Inhalant	0.217	0.257	0.843
	Pills of prescription pain relievers	-0.192	0.253	-0.761
	Age	0.000	0.001	-0.056
Sex	Female	-0.017	0.013	-1.329
Race	Black	0.068 **	0.021	3.263
	Hispanic	0.017	0.017	0.978
	Asian	-0.030	0.051	-0.594
	Other	-0.041 *	0.018	-2.232
Parental Education	6th grade	-0.026	0.278	-0.093
	7th grade	0.105	0.313	0.334
	8th grade	0.007	0.297	0.024
	9th grade	-0.001	0.265	-0.005
	10th grade	0.122	0.263	0.463
	11th grade	0.009	0.262	0.035
	12th grade	-0.018	0.263	-0.068
	High school graduate	0.060	0.258	0.231
	GED or dquivalend Diploma	0.081	0.260	0.310
	Some college	0.034	0.258	0.131
	Associate degree: Occupational	0.065	0.258	0.250
	Associate degree: Academic Program	0.052	0.259	0.200
	Bachelor's degree	0.036	0.258	0.139
	Master's degree	0.054	0.258	0.209
	Professional School degree	0.061	0.260	0.233
	Doctoral degree	0.089	0.260	0.342
Household Income	$5,000 - $11,999	-0.041	0.045	-0.922
	$12,000 - $15,999	-0.012	0.048	-0.241
	$16,000 - $24,999	-0.003	0.043	-0.059
	$25,000 - 34,999	0.055	0.040	1.356
	$35,000 - $49,999	0.039	0.039	1.003
	$50,000 - $74,999	0.061	0.039	1.540
	$75,000 - 99,999	0.071	0.040	1.769
	$100,000- $199,999	0.057	0.040	1.406
	$200,000 and greater	0.069	0.044	1.573
Parent Marriage	Widowed	0.006	0.070	0.084
	Divorced	0.045 **	0.017	2.682
	Separated	0.019	0.026	0.745
	Never married	0.038	0.023	1.667
	Living with partner	0.020	0.028	0.723
Research Site	site 3	0.013	0.031	0.407
	site 4	0.033	0.032	1.051
	site 5	-0.060	0.036	-1.699
	site 6	-0.018	0.030	-0.613
	site 7	-0.022	0.037	-0.602
	site 8	0.103 *	0.050	2.046
	site 9	-0.042	0.034	-1.253
	site 10	0.019	0.032	0.597
	site 11	-0.015	0.033	-0.440
	site 12	-0.056	0.032	-1.753
	site 13	0.012	0.032	0.365
	site 14	-0.008	0.030	-0.271
	site 15	-0.049	0.035	-1.393
	site 16	-0.013	0.026	-0.510
	site 18	0.007	0.040	0.180
	site 20	0.012	0.029	0.406
	site 21	-0.005	0.031	-0.165
	site 22	0.010	0.093	0.104
	sMRI volume	0.011	0.007	1.507

*** p < .001, ** p < .01, * p < .05

Figure A.15: The results of the analysis of the influence of the ELS. The group included children who scored more than 50 percentile of the ELS scale.

ELS1, SST correct stop vs incorrect stop, left rostral ACC — N = 2258

		Coefficient	SE	t-value
	(Intercept)	-0.188	0.283	-0.665
Prenatal	Nicotine	-0.005	0.006	-0.794
	Alcohol	0.013	0.008	1.652
	Nicotine x Alcohol	-0.024 *	0.011	-2.104
Lifetime Drug Use	Alcohol	0.590 **	0.195	3.032
	Cigarette	0.614	1.778	0.345
	E-cigarette	-0.032	0.117	-0.277
	Cigar	-0.079	0.164	-0.482
	Hookah	-0.117	0.135	-0.868
	Chew (smokeless tobacco)	0.906 *	0.450	2.015
	Pipes	-0.256	0.160	-1.601
	Inhalant	0.080	0.265	0.302
	Pills of prescription pain relievers	-0.010	0.261	-0.038
	Age	0.000	0.001	0.072
Sex	Female	0.016	0.013	1.210
Race	Black	0.034	0.022	1.559
	Hispanic	-0.005	0.018	-0.301
	Asian	-0.007	0.053	-0.126
	Other	-0.012	0.019	-0.618
Parental Education	6th grade	0.094	0.287	0.329
	7th grade	0.084	0.323	0.261
	8th grade	-0.049	0.307	-0.158
	9th grade	0.069	0.273	0.253
	10th grade	0.047	0.272	0.174
	11th grade	0.020	0.271	0.073
	12th grade	0.076	0.271	0.279
	High school graduate	0.071	0.267	0.268
	GED or dquivalend Diploma	0.155	0.268	0.579
	Some college	0.067	0.266	0.250
	Associate degree: Occupational	0.089	0.267	0.332
	Associate degree: Academic Program	0.090	0.267	0.335
	Bachelor's degree	0.065	0.266	0.244
	Master's degree	0.112	0.267	0.421
	Professional School degree	0.076	0.268	0.285
	Doctoral degree	0.072	0.268	0.268
Household Income	$5,000 - $11,999	-0.029	0.046	-0.635
	$12,000 - $15,999	0.096	0.050	1.937
	$16,000 - $24,999	0.040	0.045	0.890
	$25,000 - 34,999	0.087 *	0.042	2.073
	$35,000 - $49,999	0.085 *	0.041	2.091
	$50,000 - $74,999	0.075	0.041	1.846
	$75,000 - 99,999	0.101 *	0.042	2.416
	$100,000- $199,999	0.087 *	0.042	2.088
	$200,000 and greater	0.089	0.045	1.960
Parent Marriage	Widowed	0.007	0.074	0.093
	Divorced	0.025	0.017	1.415
	Separated	0.008	0.027	0.294
	Never married	0.032	0.024	1.323
	Living with partner	-0.020	0.028	-0.703
Research Site	site 3	0.039	0.032	1.191
	site 4	0.025	0.033	0.754
	site 5	-0.021	0.037	-0.561
	site 6	0.041	0.031	1.344
	site 7	-0.011	0.038	-0.281
	site 8	0.047	0.052	0.916
	site 9	-0.004	0.035	-0.120
	site 10	0.042	0.034	1.254
	site 11	0.018	0.035	0.519
	site 12	0.010	0.033	0.304
	site 13	0.010	0.033	0.317
	site 14	0.021	0.031	0.666
	site 15	0.031	0.036	0.848
	site 16	0.031	0.026	1.159
	site 18	0.029	0.041	0.698
	site 20	0.012	0.030	0.389
	site 21	0.010	0.032	0.319
	site 22	0.147	0.096	1.529
	sMRI volume	0.000	0.007	0.016

*** p < .001, ** p < .01, * p < .05

ELS1, SST correct stop vs incorrect stop, right rostral ACC — N = 2257

		Coefficient	SE	t-value
	(Intercept)	-0.121	0.270	-0.448
Prenatal	Nicotine	-0.004	0.006	-0.764
	Alcohol	0.016 *	0.008	2.078
	Nicotine x Alcohol	-0.021	0.011	-1.960
Lifetime Drug Use	Alcohol	0.305	0.186	1.646
	Cigarette	0.558	1.696	0.329
	E-cigarette	-0.020	0.112	-0.181
	Cigar	0.080	0.157	0.509
	Hookah	-0.062	0.129	-0.485
	Chew (smokeless tobacco)	1.037 *	0.429	2.417
	Pipes	-0.299	0.153	-1.959
	Inhalant	0.063	0.253	0.248
	Pills of prescription pain relievers	-0.022	0.249	-0.089
	Age	0.000	0.001	-0.214
Sex	Female	0.011	0.012	0.921
Race	Black	0.020	0.021	0.986
	Hispanic	-0.019	0.017	-1.113
	Asian	-0.043	0.050	-0.855
	Other	-0.021	0.018	-1.148
Parental Education	6th grade	0.078	0.274	0.283
	7th grade	0.172	0.308	0.559
	8th grade	-0.014	0.293	-0.047
	9th grade	0.029	0.261	0.111
	10th grade	0.054	0.259	0.209
	11th grade	-0.041	0.258	-0.160
	12th grade	0.195	0.259	0.753
	High school graduate	0.072	0.254	0.284
	GED or dquivalend Diploma	0.096	0.256	0.375
	Some college	0.052	0.254	0.205
	Associate degree: Occupational	0.072	0.255	0.282
	Associate degree: Academic Program	0.064	0.255	0.250
	Bachelor's degree	0.051	0.254	0.200
	Master's degree	0.079	0.254	0.311
	Professional School degree	0.034	0.256	0.134
	Doctoral degree	0.036	0.256	0.141
Household Income	$5,000 - $11,999	-0.033	0.044	-0.752
	$12,000 - $15,999	0.092	0.047	1.943
	$16,000 - $24,999	0.014	0.043	0.334
	$25,000 - 34,999	0.069	0.040	1.739
	$35,000 - $49,999	0.078 *	0.039	1.993
	$50,000 - $74,999	0.052	0.039	1.335
	$75,000 - 99,999	0.082 *	0.040	2.057
	$100,000- $199,999	0.079 *	0.040	1.979
	$200,000 and greater	0.089 *	0.043	2.054
Parent Marriage	Widowed	0.043	0.070	0.607
	Divorced	0.022	0.017	1.312
	Separated	-0.008	0.025	-0.302
	Never married	0.011	0.023	0.463
	Living with partner	-0.046	0.027	-1.686
Research Site	site 3	0.033	0.031	1.058
	site 4	0.043	0.031	1.366
	site 5	-0.003	0.035	-0.079
	site 6	0.040	0.029	1.370
	site 7	-0.020	0.036	-0.552
	site 8	0.037	0.049	0.753
	site 9	0.019	0.033	0.574
	site 10	0.015	0.032	0.469
	site 11	0.006	0.033	0.178
	site 12	0.020	0.031	0.622
	site 13	0.032	0.031	1.020
	site 14	0.014	0.030	0.460
	site 15	0.048	0.035	1.381
	site 16	0.022	0.025	0.891
	site 18	0.057	0.039	1.439
	site 20	0.004	0.028	0.150
	site 21	0.014	0.031	0.455
	site 22	0.128	0.092	1.397
	sMRI volume	0.000	0.007	-0.050

*** p < .001, ** p < .01, * p < .05

Figure A.16: The results of the analysis of the influence of the ELS. The group included children who scored more than 50 percentile of the ELS scale.

ELS1, SST correct stop vs correct go, right pars triangularis				N = 2258
		Coefficient	SE	t-value
	(Intercept)	-0.088	0.244	-0.361
Prenatal	Nicotine	0.011 ***	0.005	2.072
	Alcohol	-0.002 ***	0.007	-0.221
	Nicotine x Alcohol	-0.007 ***	0.010	-0.750
Lifetime Drug Use	Alcohol	-0.016	0.069	-0.229
	Cigarette	0.403	1.534	0.263
	E-cigarette	-0.017	0.101	-0.165
	Cigar	0.120	0.119	1.008
	Hookah	0.024	0.116	0.202
	Chew (smokeless tobacco)	-0.108	0.196	-0.552
	Pipes	0.041	0.093	0.442
	Inhalant	0.247	0.229	1.078
	Pills of prescription pain relievers	-0.179	0.225	-0.793
	Age	0.001	0.001	1.100
Sex	Female	-0.002	0.011	-0.216
Race	Black	0.026	0.019	1.380
	Hispanic	-0.003	0.015	-0.166
	Asian	-0.033	0.046	-0.721
	Other	-0.044 **	0.016	-2.653
Parental Education	6th grade	0.008	0.248	0.031
	7th grade	0.104	0.279	0.373
	8th grade	-0.019	0.265	-0.071
	9th grade	0.089	0.236	0.376
	10th grade	0.089	0.235	0.378
	11th grade	0.053	0.234	0.228
	12th grade	0.092	0.235	0.392
	High school graduate	0.127	0.230	0.551
	GED or dquivalend Diploma	0.132	0.232	0.570
	Some college	0.095	0.230	0.414
	Associate degree: Occupational	0.124	0.230	0.536
	Associate degree: Academic Program	0.092	0.231	0.397
	Bachelor's degree	0.105	0.230	0.457
	Master's degree	0.112	0.230	0.485
	Professional School degree	0.125	0.232	0.540
	Doctoral degree	0.141	0.232	0.609
Household Income	$5,000 - $11,999	-0.060	0.040	-1.506
	$12,000 - $15,999	-0.006	0.043	-0.132
	$16,000 - $24,999	-0.052	0.039	-1.358
	$25,000 - 34,999	-0.028	0.036	-0.768
	$35,000 - $49,999	-0.017	0.035	-0.487
	$50,000 - $74,999	-0.004	0.035	-0.117
	$75,000 - 99,999	0.007	0.036	0.190
	$100,000- $199,999	-0.013	0.036	-0.352
	$200,000 and greater	-0.001	0.039	-0.026
Parent Marriage	Widowed	0.025	0.062	0.394
	Divorced	0.012	0.015	0.827
	Separated	0.017	0.023	0.762
	Never married	0.044 *	0.021	2.163
	Living with partner	0.061 *	0.025	2.462
Research Site	site 3	0.006	0.028	0.217
	site 4	0.001	0.028	0.042
	site 5	-0.084 **	0.032	-2.646
	site 6	-0.043	0.026	-1.640
	site 7	-0.036	0.033	-1.112
	site 8	0.013	0.045	0.281
	site 9	-0.040	0.030	-1.346
	site 10	-0.003	0.029	-0.103
	site 11	-0.044	0.030	-1.473
	site 12	-0.066 *	0.028	-2.312
	site 13	-0.046	0.028	-1.645
	site 14	-0.047	0.027	-1.766
	site 15	-0.077 *	0.031	-2.433
	site 16	-0.010	0.023	-0.424
	site 18	-0.014	0.036	-0.395
	site 20	-0.041	0.026	-1.615
	site 21	-0.024	0.028	-0.885
	site 22	-0.024	0.083	-0.288
	sMRI volume	0.005	0.006	0.848

*** p < .001, ** p < .01, * p < .05

Figure A.17: The results of the analysis of the influence of the ELS. The group included children who scored more than 50 percentile of the ELS scale.

ELS0, SST correct stop vs correct go, right caudal ACC — N = 2640

		Coefficient	SE	t-value
	(Intercept)	-0.019	0.163	-0.115
Prenatal	Nicotine	0.003	0.003	0.902
	Alcohol	-0.001	0.003	-0.442
	Nicotine x Alcohol	0.004 *	0.002	2.553
Lifetime Drug Use	Alcohol	-0.152	0.089	-1.712
	Cigarette	0.075	0.215	0.349
	Hookah	-0.043	0.069	-0.629
	Chew (smokeless tobacco)	0.141	0.153	0.918
	Pipes	0.101	0.160	0.628
	Age	0.000	0.000	0.447
Sex	Female	-0.002	0.007	-0.239
Race	Black	-0.001	0.014	-0.093
	Hispanic	-0.002	0.010	-0.222
	Asian	0.017	0.023	0.735
	Other	-0.008	0.011	-0.779
Parental Education	3th grade	-0.065	0.217	-0.298
	6th grade	0.189	0.187	1.012
	7th grade	0.202	0.218	0.927
	8th grade	0.191	0.166	1.149
	9th grade	0.101	0.160	0.629
	10th grade	0.097	0.159	0.610
	11th grade	0.171	0.157	1.090
	12th grade	0.096	0.158	0.608
	High school graduate	0.107	0.154	0.696
	GED or dquivalend Diploma	0.123	0.157	0.788
	Some college	0.119	0.154	0.774
	Associate degree: Occupational	0.108	0.154	0.698
	Associate degree: Academic Program	0.121	0.155	0.782
	Bachelor's degree	0.120	0.154	0.781
	Master's degree	0.107	0.154	0.697
	Professional School degree	0.109	0.155	0.703
	Doctoral degree	0.107	0.155	0.693
Household Income	$5,000 - $11,999	-0.066 *	0.033	-1.972
	$12,000 - $15,999	-0.028	0.032	-0.859
	$16,000 - $24,999	-0.055	0.030	-1.852
	$25,000 - 34,999	-0.032	0.028	-1.116
	$35,000 - $49,999	-0.046	0.027	-1.680
	$50,000 - $74,999	-0.053 *	0.026	-2.003
	$75,000 - 99,999	-0.045	0.026	-1.709
	$100,000- $199,999	-0.046	0.026	-1.744
	$200,000 and greater	-0.047	0.027	-1.717
Parent Marriage	Widowed	-0.071	0.045	-1.582
	Divorced	0.002	0.018	0.084
	Separated	0.044	0.025	1.737
	Never married	0.012	0.016	0.764
	Living with partner	0.011	0.017	0.633
Research Site	site 3	-0.002	0.018	-0.115
	site 4	0.021	0.019	1.081
	site 5	0.000	0.018	-0.012
	site 6	-0.011	0.016	-0.702
	site 7	-0.005	0.021	-0.265
	site 8	0.007	0.021	0.345
	site 9	-0.014	0.017	-0.829
	site 10	0.015	0.018	0.852
	site 11	-0.014	0.021	-0.635
	site 12	-0.028	0.016	-1.706
	site 13	-0.002	0.017	-0.126
	site 14	0.007	0.015	0.449
	site 15	-0.028	0.023	-1.183
	site 16	0.005	0.014	0.355
	site 18	-0.022	0.019	-1.135
	site 20	-0.017	0.015	-1.111
	site 21	-0.003	0.016	-0.181
	site 22	0.019	0.048	0.398
	sMRI volume	0.007	0.004	1.862

*** $p < .001$, ** $p < .01$, * $p < .05$

ELS0, SST correct stop vs incorrect stop, right caudal ACC — N = 2638

		Coefficient	SE	t-value
	(Intercept)	-0.023	0.196	-0.115
Prenatal	Nicotine	0.000	0.004	0.027
	Alcohol	-0.006	0.004	-1.590
	Nicotine x Alcohol	0.005 *	0.002	2.328
Lifetime Drug Use	Alcohol	-0.018	0.106	-0.171
	Cigarette	-2.006	1.832	-1.095
	Hookah	-0.032	0.082	-0.395
	Pipes	-0.037	0.192	-0.194
	Age	0.000	0.000	0.776
Sex	Female	-0.018 *	0.008	-2.130
Race	Black	0.000	0.017	0.004
	Hispanic	-0.006	0.012	-0.474
	Asian	0.014	0.027	0.510
	Other	-0.005	0.013	-0.391
Parental Education	3th grade	-0.320	0.260	-1.230
	6th grade	-0.013	0.224	-0.059
	7th grade	0.111	0.261	0.424
	8th grade	-0.032	0.199	-0.163
	9th grade	-0.035	0.192	-0.180
	10th grade	-0.024	0.191	-0.124
	11th grade	0.045	0.188	0.238
	12th grade	-0.014	0.189	-0.074
	High school graduate	-0.016	0.185	-0.089
	GED or dquivalend Diploma	0.058	0.187	0.309
	Some college	0.002	0.184	0.013
	Associate degree: Occupational	-0.009	0.185	-0.046
	Associate degree: Academic Program	0.003	0.185	0.014
	Bachelor's degree	0.006	0.185	0.031
	Master's degree	-0.023	0.185	-0.124
	Professional School degree	0.000	0.185	-0.001
	Doctoral degree	-0.028	0.185	-0.151
Household Income	$5,000 - $11,999	-0.016	0.040	-0.394
	$12,000 - $15,999	-0.019	0.038	-0.497
	$16,000 - $24,999	-0.040	0.036	-1.112
	$25,000 - 34,999	-0.011	0.034	-0.328
	$35,000 - $49,999	-0.004	0.033	-0.107
	$50,000 - $74,999	-0.018	0.032	-0.566
	$75,000 - 99,999	-0.018	0.032	-0.575
	$100,000- $199,999	-0.019	0.032	-0.600
	$200,000 and greater	-0.009	0.033	-0.275
Parent Marriage	Widowed	-0.134 *	0.053	-2.513
	Divorced	-0.026	0.022	-1.169
	Separated	0.022	0.030	0.715
	Never married	-0.021	0.019	-1.095
	Living with partner	0.035	0.021	1.712
Research Site	site 3	0.005	0.022	0.236
	site 4	0.018	0.023	0.799
	site 5	-0.008	0.022	-0.387
	site 6	-0.004	0.019	-0.204
	site 7	0.012	0.025	0.505
	site 8	-0.038	0.025	-1.558
	site 9	-0.036	0.021	-1.723
	site 10	0.028	0.022	1.288
	site 11	0.034	0.026	1.345
	site 12	-0.035	0.020	-1.774
	site 13	0.017	0.020	0.853
	site 14	0.031	0.018	1.772
	site 15	-0.006	0.028	-0.205
	site 16	-0.004	0.016	-0.274
	site 18	0.001	0.023	0.033
	site 20	-0.015	0.019	-0.809
	site 21	0.010	0.019	0.512
	site 22	0.037	0.057	0.652
	sMRI volume	0.001	0.005	0.213

*** $p < .001$, ** $p < .01$, * $p < .05$

Figure A.18: The results of the analysis of the influence of the ELS. The group included children who scored less than 50 percentile of the ELS scale.

ELS0, SST correct stop vs incorrect stop, right pars opercularis — N = 2637

		Coefficient	SE	t-value
	(Intercept)	-0.018	0.194	-0.094
Prenatal	Nicotine	0.000	0.004	-0.131
	Alcohol	-0.008 *	0.004	-2.269
	Nicotine x Alcohol	-0.005	0.005	-0.997
Lifetime Drug Use	Alcohol	0.029	0.105	0.275
	Cigar	-1.963	1.815	-1.081
	Hookah	-0.022	0.082	-0.273
	Pipes	-0.247	0.190	-1.301
	Age	0.001 **	0.000	2.777
Sex	Female	-0.018 *	0.008	-2.201
Race	Black	0.014	0.017	0.823
	Hispanic	0.000	0.012	0.036
	Asian	0.036	0.027	1.323
	Other	-0.012	0.013	-0.971
Parental Education	3th grade	-0.391	0.258	-1.517
	6th grade	-0.179	0.222	-0.806
	7th grade	-0.029	0.259	-0.113
	8th grade	-0.139	0.197	-0.708
	9th grade	-0.152	0.190	-0.800
	10th grade	-0.173	0.189	-0.914
	11th grade	-0.104	0.186	-0.557
	12th grade	-0.165	0.187	-0.881
	High school graduate	-0.105	0.183	-0.574
	GED or dquivalend Diploma	-0.081	0.186	-0.434
	Some college	-0.126	0.183	-0.692
	Associate degree: Occupational	-0.117	0.183	-0.638
	Associate degree: Academic Program	-0.114	0.183	-0.622
	Bachelor's degree	-0.121	0.183	-0.661
	Master's degree	-0.139	0.183	-0.760
	Professional School degree	-0.127	0.184	-0.689
	Doctoral degree	-0.119	0.184	-0.647
Household Income	$5,000 - $11,999	-0.040	0.040	-1.010
	$12,000 - $15,999	-0.042	0.038	-1.108
	$16,000 - $24,999	-0.015	0.035	-0.439
	$25,000 - 34,999	-0.039	0.034	-1.160
	$35,000 - $49,999	-0.005	0.032	-0.140
	$50,000 - $74,999	-0.018	0.031	-0.588
	$75,000 - 99,999	-0.015	0.031	-0.487
	$100,000- $199,999	-0.026	0.031	-0.842
	$200,000 and greater	-0.021	0.032	-0.660
Parent Marriage	Widowed	-0.074	0.053	-1.399
	Divorced	0.006	0.022	0.276
	Separated	-0.042	0.030	-1.397
	Never married	-0.013	0.019	-0.719
	Living with partner	0.052 *	0.021	2.538
Research Site	site 3	0.006	0.021	0.294
	site 4	0.028	0.023	1.219
	site 5	0.000	0.021	-0.015
	site 6	-0.006	0.019	-0.346
	site 7	0.027	0.024	1.099
	site 8	-0.004	0.024	-0.165
	site 9	-0.024	0.021	-1.159
	site 10	0.030	0.021	1.400
	site 11	0.031	0.025	1.235
	site 12	-0.008	0.019	-0.423
	site 13	0.015	0.020	0.789
	site 14	0.025	0.017	1.409
	site 15	-0.006	0.028	-0.210
	site 16	0.004	0.016	0.251
	site 18	0.028	0.023	1.228
	site 20	-0.010	0.018	-0.543
	site 21	0.023	0.019	1.184
	site 22	0.017	0.056	0.308
	sMRI volume	0.002	0.005	0.381

*** p < .001, ** p < .01, * p < .05

ELS0, SST correct stop vs incorrect stop, left pars opercularis — N = 2638

		Coefficient	SE	t-value
	(Intercept)	0.109	0.183	0.593
Prenatal	Nicotine	0.000	0.003	0.129
	Alcohol	-0.008 *	0.004	-2.354
	Nicotine x Alcohol	0.003	0.002	1.733
Lifetime Drug Use	Alcohol	0.045	0.099	0.454
	Cigarette	-2.189	1.717	-1.275
	Hookah	-0.058	0.077	-0.746
	Pipes	-0.175	0.180	-0.974
	Age	0.000	0.000	0.776
Sex	Female	-0.018 *	0.008	-2.337
Race	Black	-0.001	0.016	-0.063
	Hispanic	-0.008	0.012	-0.690
	Asian	0.016	0.026	0.637
	Other	-0.010	0.012	-0.792
Parental Education	3th grade	-0.406	0.244	-1.668
	6th grade	-0.042	0.210	-0.200
	7th grade	-0.065	0.245	-0.266
	8th grade	-0.162	0.186	-0.872
	9th grade	-0.148	0.180	-0.825
	10th grade	-0.156	0.179	-0.870
	11th grade	-0.082	0.176	-0.464
	12th grade	-0.134	0.177	-0.758
	High school graduate	-0.132	0.173	-0.765
	GED or dquivalend Diploma	-0.092	0.176	-0.524
	Some college	-0.147	0.173	-0.851
	Associate degree: Occupational	-0.152	0.173	-0.876
	Associate degree: Academic Program	-0.126	0.173	-0.727
	Bachelor's degree	-0.141	0.173	-0.814
	Master's degree	-0.154	0.173	-0.891
	Professional School degree	-0.132	0.174	-0.761
	Doctoral degree	-0.145	0.174	-0.836
Household Income	$5,000 - $11,999	-0.070	0.038	-1.858
	$12,000 - $15,999	-0.039	0.036	-1.082
	$16,000 - $24,999	-0.032	0.033	-0.975
	$25,000 - 34,999	-0.038	0.032	-1.201
	$35,000 - $49,999	-0.017	0.031	-0.538
	$50,000 - $74,999	-0.033	0.030	-1.098
	$75,000 - 99,999	-0.020	0.030	-0.667
	$100,000- $199,999	-0.036	0.030	-1.228
	$200,000 and greater	-0.025	0.031	-0.800
Parent Marriage	Widowed	-0.042	0.050	-0.840
	Divorced	-0.009	0.021	-0.450
	Separated	-0.024	0.028	-0.865
	Never married	0.003	0.018	0.185
	Living with partner	0.043 *	0.019	2.219
Research Site	site 3	0.016	0.020	0.795
	site 4	0.039	0.022	1.825
	site 5	0.010	0.020	0.502
	site 6	0.006	0.018	0.333
	site 7	0.026	0.023	1.138
	site 8	0.002	0.023	0.107
	site 9	-0.016	0.019	-0.831
	site 10	0.033	0.020	1.638
	site 11	0.033	0.024	1.376
	site 12	-0.011	0.018	-0.582
	site 13	0.015	0.019	0.822
	site 14	0.021	0.016	1.284
	site 15	-0.005	0.026	-0.200
	site 16	0.006	0.015	0.375
	site 18	0.046 *	0.022	2.105
	site 20	0.006	0.017	0.317
	site 21	0.019	0.018	1.070
	site 22	0.034	0.053	0.639
	sMRI volume	0.005	0.004	1.164

*** p < .001, ** p < .01, * p < .05

Figure A.19: The results of the analysis on the influence of the ELS. The group included children who scored less than 50 percentile of the ELS scale.

ELS0, SST correct stop vs incorrect stop, left pars triagularis — N = 2638

		Coefficient	SE	t-value
	(Intercept)	0.275	0.244	1.131
Prenatal	Nicotine	0.003	0.005	0.673
	Alcohol	-0.012 **	0.005	-2.602
	Nicotine x Alcohol	0.004	0.002	1.522
Lifetime Drug Use	Alcohol	0.037	0.132	0.277
	Cigar	-2.585	2.278	-1.135
	Hookah	-0.075	0.102	-0.729
	Pipes	-0.156	0.239	-0.654
Age		0.000	0.001	0.370
Sex	Female	-0.008	0.010	-0.731
Race	Black	0.010	0.021	0.488
	Hispanic	-0.010	0.015	-0.627
	Asian	0.058	0.034	1.721
	Other	0.012	0.016	0.753
Parental Education	3th grade	-0.568	0.323	-1.755
	6th grade	-0.055	0.278	-0.197
	7th grade	-0.303	0.325	-0.933
	8th grade	-0.311	0.247	-1.260
	9th grade	-0.224	0.239	-0.938
	10th grade	-0.249	0.238	-1.046
	11th grade	-0.157	0.234	-0.671
	12th grade	-0.221	0.235	-0.940
	High school graduate	-0.238	0.230	-1.038
	GED or dquivalend Diploma	-0.202	0.233	-0.868
	Some college	-0.255	0.229	-1.114
	Associate degree: Occupational	-0.247	0.230	-1.073
	Associate degree: Academic Program	-0.217	0.230	-0.941
	Bachelor's degree	-0.250	0.229	-1.088
	Master's degree	-0.268	0.230	-1.168
	Professional School degree	-0.216	0.231	-0.939
	Doctoral degree	-0.267	0.230	-1.161
Household Income	$5,000 - $11,999	-0.096	0.050	-1.921
	$12,000 - $15,999	-0.045	0.048	-0.940
	$16,000 - $24,999	-0.018	0.044	-0.413
	$25,000 - 34,999	-0.060	0.042	-1.404
	$35,000 - $49,999	-0.053	0.041	-1.309
	$50,000 - $74,999	-0.062	0.039	-1.569
	$75,000 - 99,999	-0.044	0.039	-1.108
	$100,000- $199,999	-0.056	0.039	-1.427
	$200,000 and greater	-0.051	0.041	-1.247
Parent Marriage	Widowed	-0.088	0.066	-1.321
	Divorced	0.016	0.027	0.578
	Separated	-0.005	0.037	-0.123
	Never married	0.002	0.023	0.095
	Living with partner	0.036	0.026	1.388
Research Site	site 3	0.002	0.027	0.074
	site 4	0.035	0.029	1.239
	site 5	-0.014	0.027	-0.512
	site 6	-0.012	0.023	-0.529
	site 7	0.007	0.031	0.214
	site 8	-0.015	0.031	-0.496
	site 9	-0.051	0.026	-1.956
	site 10	0.007	0.027	0.269
	site 11	0.028	0.032	0.872
	site 12	-0.048 *	0.024	-1.968
	site 13	0.001	0.025	0.027
	site 14	0.007	0.022	0.313
	site 15	-0.073 *	0.035	-2.118
	site 16	0.000	0.020	0.006
	site 18	0.055	0.029	1.896
	site 20	0.040	0.023	1.754
	site 21	0.007	0.024	0.286
	site 22	0.029	0.071	0.411
sMRI volume		0.008	0.006	1.294

*** p < .001, ** p < .01, * p < .05

ELS0, SST correct stop vs incorrect stop, right pars triagularis — N = 2637

		Coefficient	SE	t-value
	(Intercept)	0.042 ***	0.239	0.176
Prenatal	Nicotine	-0.001	0.005	-0.272
	Alcohol	-0.013 **	0.005	-2.923
	Nicotine x Alcohol	-0.006	0.007	-0.948
Lifetime Drug Use	Alcohol	0.031	0.129	0.243
	Cigar	-1.820	2.232	-0.816
	Hookah	-0.054	0.100	-0.541
	Pipes	-0.234	0.234	-1.001
Age		0.001	0.001	1.807
Sex	Female	-0.014	0.010	-1.344
Race	Black	0.014	0.021	0.684
	Hispanic	-0.021	0.015	-1.415
	Asian	0.074 *	0.033	2.221
	Other	-0.004	0.016	-0.241
Parental Education	3th grade	-0.376	0.317	-1.188
	6th grade	-0.106	0.273	-0.390
	7th grade	-0.043	0.318	-0.134
	8th grade	-0.159	0.242	-0.655
	9th grade	-0.190	0.234	-0.813
	10th grade	-0.122	0.233	-0.525
	11th grade	-0.094	0.229	-0.410
	12th grade	-0.146	0.230	-0.635
	High school graduate	-0.134	0.225	-0.595
	GED or dquivalend Diploma	-0.099	0.228	-0.433
	Some college	-0.144	0.225	-0.640
	Associate degree: Occupational	-0.124	0.225	-0.551
	Associate degree: Academic Program	-0.120	0.226	-0.530
	Bachelor's degree	-0.148	0.225	-0.658
	Master's degree	-0.183	0.225	-0.815
	Professional School degree	-0.165	0.226	-0.730
	Doctoral degree	-0.180	0.226	-0.796
Household Income	$5,000 - $11,999	-0.011	0.049	-0.221
	$12,000 - $15,999	-0.006	0.047	-0.119
	$16,000 - $24,999	-0.001	0.043	-0.024
	$25,000 - 34,999	-0.014	0.042	-0.338
	$35,000 - $49,999	-0.002	0.040	-0.053
	$50,000 - $74,999	-0.009	0.039	-0.223
	$75,000 - 99,999	0.007	0.039	0.181
	$100,000- $199,999	-0.006	0.038	-0.157
	$200,000 and greater	0.006	0.040	0.150
Parent Marriage	Widowed	-0.084	0.065	-1.291
	Divorced	-0.023	0.027	-0.850
	Separated	-0.065	0.037	-1.764
	Never married	-0.037	0.023	-1.635
	Living with partner	0.074 **	0.025	2.922
Research Site	site 3	0.018	0.026	0.677
	site 4	0.035	0.028	1.250
	site 5	0.005	0.026	0.193
	site 6	-0.029	0.023	-1.286
	site 7	0.009	0.030	0.288
	site 8	-0.008	0.030	-0.280
	site 9	-0.071 **	0.025	-2.816
	site 10	0.037	0.026	1.414
	site 11	0.034	0.031	1.078
	site 12	-0.033	0.024	-1.370
	site 13	0.003	0.024	0.126
	site 14	0.030	0.021	1.405
	site 15	-0.044	0.034	-1.297
	site 16	-0.004	0.020	-0.179
	site 18	0.041	0.028	1.443
	site 20	0.003	0.023	0.134
	site 21	0.022	0.023	0.934
	site 22	0.025	0.069	0.359
sMRI volume		0.002	0.006	0.302

*** p < .001, ** p < .01, * p < .05

Figure A.20: The results of the analysis on the influence of the ELS. The group included children who scored less than 50 percentile of the ELS scale.

Left table:

Ohter, MID reward receipt, left accumbens area				N = 540
		Coefficient	SE	t-value
	(Intercept)	-0.148	0.411	-0.360
Prenatal	Nicotine	-0.044 *	0.021	-2.084
	Alcohol	-0.026	0.018	-1.435
	Nicotine x Alcohol	-0.211 **	0.071	-2.952
Lifetime Drug Use	E-cigarette	3.419 ***	0.413	8.281
	Chew (smokeless tobacco)	-0.602	0.328	-1.834
	Age	0.001	0.002	0.313
Sex	Female	-0.019	0.032	-0.595
Parental Education	9th grade	0.943 *	0.470	2.008
	10th grade	0.180	0.421	0.426
	11th grade	-0.031	0.386	-0.080
	12th grade	0.304	0.372	0.818
	High school graduate	0.297	0.337	0.882
	GED or dquivalend Diploma	0.104	0.347	0.301
	Some college	0.291	0.333	0.875
	Associate degree: Occupational	0.362	0.336	1.079
	Associate degree: Academic Program	0.344	0.337	1.019
	Bachelor's degree	0.350	0.333	1.052
	Master's degree	0.310	0.335	0.928
	Professional School degree	0.377	0.339	1.114
	Doctoral degree	0.176	0.341	0.516
Household Income	$5,000 - $11,999	-0.025	0.117	-0.218
	$12,000 - $15,999	0.052	0.124	0.418
	$16,000 - $24,999	0.066	0.117	0.568
	$25,000 - 34,999	-0.039	0.118	-0.335
	$35,000 - $49,999	-0.014	0.107	-0.133
	$50,000 - $74,999	-0.047	0.103	-0.453
	$75,000 - 99,999	-0.103	0.106	-0.974
	$100,000- $199,999	-0.058	0.105	-0.556
	$200,000 and greater	-0.029	0.111	-0.260
Parent Marriage	Widowed	0.029	0.189	0.152
	Divorced	0.089	0.054	1.659
	Separated	0.027	0.086	0.314
	Never married	0.030	0.061	0.486
	Living with partner	-0.006	0.067	-0.089
Research Site	site 3	-0.064	0.119	-0.532
	site 4	0.032	0.071	0.445
	site 5	-0.030	0.095	-0.313
	site 6	-0.025	0.070	-0.362
	site 7	-0.061	0.106	-0.578
	site 8	-0.052	0.086	-0.600
	site 9	0.010	0.072	0.131
	site 10	-0.224 **	0.085	-2.640
	site 11	-0.046	0.089	-0.510
	site 12	-0.106	0.076	-1.394
	site 13	-0.152 *	0.073	-2.076
	site 14	0.028	0.072	0.381
	site 15	0.128	0.092	1.390
	site 16	-0.004	0.068	-0.056
	site 18	0.069	0.100	0.684
	site 20	-0.056	0.075	-0.744
	site 21	-0.036	0.078	-0.466
	site 22	-0.242	0.192	-1.265
	sMRI volume	0.003	0.018	0.152

*** p < .001, ** p < .01, * p < .05

Right table:

White, SST correct stop vs correct go, caudal ACC				N = 3181
		Coefficient	SE	t-value
	(Intercept)	0.057	0.082	0.686
Prenatal	Nicotine	0.004	0.003	1.357
	Alcohol	-0.002	0.004	-0.608
	Nicotine x Alcohol	0.004 ***	0.001	4.386
Lifetime Drug Use	Alcohol	-0.021	0.041	-0.518
	E-cigarette	0.017	0.010	1.713
	Cigar	0.092	0.073	1.258
	Hookah	-0.014	0.066	-0.205
	Chew (smokeless tobacco)	0.136	0.106	1.280
	Pipes	-0.044	0.054	-0.817
	Edible(marijuana in food)	-0.142	0.184	-0.773
	Age	0.000	0.000	-0.289
Sex	Female	0.003	0.006	0.432
Parental Education	10th grade	-0.111	0.087	-1.264
	11th grade	-0.025	0.103	-0.243
	12th grade	-0.037	0.102	-0.357
	High school graduate	-0.047	0.059	-0.791
	GED or dquivalend Diploma	-0.058	0.064	-0.901
	Some college	-0.034	0.058	-0.588
	Associate degree: Occupational	-0.028	0.059	-0.473
	Associate degree: Academic Program	-0.026	0.059	-0.447
	Bachelor's degree	-0.041	0.058	-0.705
	Master's degree	-0.040	0.058	-0.689
	Professional School degree	-0.030	0.059	-0.509
	Doctoral degree	-0.042	0.059	-0.708
Household Income	$5,000 - $11,999	0.052	0.057	0.924
	$12,000 - $15,999	0.066	0.054	1.234
	$16,000 - $24,999	0.044	0.048	0.929
	$25,000 - 34,999	0.050	0.045	1.112
	$35,000 - $49,999	0.045	0.045	1.011
	$50,000 - $74,999	0.056	0.044	1.274
	$75,000 - 99,999	0.074	0.044	1.678
	$100,000- $199,999	0.053	0.044	1.213
	$200,000 and greater	0.062	0.044	1.403
Parent Marriage	Widowed	-0.036	0.040	-0.902
	Divorced	0.002	0.011	0.160
	Separated	0.009	0.019	0.487
	Never married	0.004	0.020	0.187
	Living with partner	0.026	0.020	1.285
Research Site	site 3	0.036	0.031	1.175
	site 4	0.009	0.017	0.541
	site 5	-0.010	0.016	-0.668
	site 6	-0.005	0.013	-0.384
	site 7	0.005	0.017	0.283
	site 8	0.017	0.023	0.732
	site 9	-0.005	0.020	-0.263
	site 10	-0.008	0.020	-0.429
	site 11	-0.027	0.017	-1.579
	site 12	-0.014	0.015	-0.907
	site 13	-0.001	0.015	-0.042
	site 14	0.000	0.013	-0.026
	site 15	-0.008	0.020	-0.402
	site 16	0.008	0.011	0.745
	site 18	-0.011	0.016	-0.672
	site 20	-0.012	0.013	-0.896
	site 21	0.009	0.014	0.616
	site 22	-0.030	0.050	-0.598
	sMRI volume	0.001	0.004	0.153

*** p < .001, ** p < .01, * p < .05

Figure A.21: The results of the analysis of the influence of race and ethnicity.

Left table:

Hispanic, UPPS-P total
R squared = 0.035 N = 1751

Group	Variable	Coefficient		SE	t-value
	(Intercept)	44.740	***	6.333	7.064
Prenatal	Nicotine	0.085		0.194	0.438
	Alcohol	1.477	**	0.542	2.727
	Nicotine x Alcohol	-0.208	**	0.079	-2.616
Lifetime Drug Use	Alcohol	10.881	**	3.842	2.832
	E-cigarette	-0.993		2.891	-0.343
	Hookah	6.309		3.691	1.709
	Inhalant	1.456	*	0.593	2.453
	Pills of prescription pain relievers	9.922		7.702	1.288
	Other	-0.454	*	0.217	-2.091
	Age	-0.052	*	0.025	-2.088
Sex	Female	-2.431	***	0.425	-5.726
Parental Education	2th grade	-0.147		9.425	-0.016
	3th grade	1.053		6.442	0.163
	4th grade	1.455		6.466	0.225
	5th grade	10.889		7.772	1.401
	6th grade	2.276		5.586	0.407
	7th grade	2.154		6.026	0.357
	8th grade	2.031		5.670	0.358
	9th grade	3.170		5.530	0.573
	10th grade	4.057		5.604	0.724
	11th grade	3.505		5.548	0.632
	12th grade	2.350		5.536	0.424
	High school graduate	1.926		5.469	0.352
	GED or dquivalend Diploma	4.290		5.540	0.774
	Some college	1.455		5.465	0.266
	Associate degree: Occupational	2.127		5.487	0.388
	Associate degree: Academic Program	1.700		5.505	0.309
	Bachelor's degree	1.978		5.476	0.361
	Master's degree	1.427		5.494	0.260
	Professional School degree	1.924		5.653	0.340
	Doctoral degree	2.613		5.661	0.461
Household Income	$5,000 - $11,999	0.073		1.126	0.065
	$12,000 - $15,999	1.267		1.199	1.057
	$16,000 - $24,999	1.251		1.035	1.208
	$25,000 - 34,999	0.475		1.007	0.472
	$35,000 - $49,999	2.353	*	0.987	2.385
	$50,000 - $74,999	1.162		1.009	1.152
	$75,000 - 99,999	1.377		1.061	1.298
	$100,000- $199,999	1.145		1.073	1.067
	$200,000 and greater	1.138		1.371	0.830
Parent Marriage	Widowed	1.651		2.202	0.750
	Divorced	0.820		0.655	1.252
	Separated	-0.836		0.782	-1.069
	Never married	0.184		0.658	0.279
	Living with partner	-1.007		0.641	-1.571
Research Site	site 2	-0.389		1.005	-0.387
	site 3	-0.694		0.741	-0.937
	site 4	-0.232		0.970	-0.239
	site 5	6.834	**	2.323	2.941
	site 6	0.324		1.164	0.278
	site 7	1.516		1.503	1.009
	site 8	-1.587		1.270	-1.249
	site 9	-0.389		0.932	-0.418
	site 10	0.379		0.737	0.515
	site 11	-0.076		1.673	-0.045
	site 12	0.866		1.551	0.558
	site 13	0.196		1.317	0.149
	site 14	1.178		1.543	0.763
	site 15	1.032		2.236	0.462
	site 16	-0.328		1.076	-0.305
	site 17	-1.405		2.157	-0.652
	site 18	1.824		1.978	0.922
	site 19	1.573		1.561	1.008
	site 20	1.763		2.004	0.880
	site 21	1.734		1.031	1.683
	site 22	-2.380		3.222	-0.739
	sMRI volume	-0.343		0.245	-1.401

*** p < .001, ** p < .01, * p < .05

Right table:

Hispanic, SST correct stop vs correct go, right caudal ACC
N = 1005

Group	Variable	Coefficient		SE	t-value
	(Intercept)	-0.156		0.189	-0.826
Prenatal	Nicotine	0.003		0.006	0.545
	Alcohol	0.004		0.006	0.750
	Nicotine x Alcohol	0.029	*	0.011	2.563
Lifetime Drug Use	E-cigarette	-0.053		0.084	-0.628
	Hookah	-0.087		0.086	-1.003
	Inhalant	0.128		0.171	0.744
	Pills of prescription pain relievers	-0.091		0.167	-0.548
	Age	0.000		0.001	0.701
Sex	Female	0.002		0.012	0.152
Parental Education	3th grade	0.013		0.203	0.065
	4th grade	0.146		0.237	0.615
	6th grade	0.109		0.172	0.631
	7th grade	0.187		0.192	0.975
	8th grade	0.094		0.173	0.545
	9th grade	0.125		0.169	0.742
	10th grade	0.152		0.170	0.891
	11th grade	0.161		0.170	0.945
	12th grade	0.096		0.169	0.569
	High school graduate	0.138		0.167	0.831
	GED or dquivalend Diploma	0.157		0.169	0.932
	Some college	0.136		0.167	0.815
	Associate degree: Occupational	0.098		0.167	0.589
	Associate degree: Academic Program	0.115		0.168	0.685
	Bachelor's degree	0.142		0.167	0.849
	Master's degree	0.116		0.167	0.697
	Professional School degree	-0.001		0.171	-0.005
	Doctoral degree	0.053		0.171	0.308
Household Income	$5,000 - $11,999	-0.018		0.040	-0.451
	$12,000 - $15,999	0.041		0.039	1.061
	$16,000 - $24,999	-0.004		0.035	-0.108
	$25,000 - 34,999	0.045		0.033	1.369
	$35,000 - $49,999	0.054		0.032	1.662
	$50,000 - $74,999	0.018		0.033	0.540
	$75,000 - 99,999	0.034		0.034	1.007
	$100,000- $199,999	0.040		0.034	1.167
	$200,000 and greater	0.047		0.041	1.163
Parent Marriage	Widowed	-0.067		0.066	-1.013
	Divorced	0.010		0.019	0.533
	Separated	0.001		0.023	0.058
	Never married	0.033		0.021	1.594
	Living with partner	-0.002		0.020	-0.096
Research Site	site 3	0.019		0.022	0.871
	site 4	0.057		0.034	1.702
	site 5	-0.114		0.062	-1.841
	site 6	0.008		0.032	0.252
	site 7	-0.012		0.044	-0.271
	site 8	0.046		0.037	1.240
	site 9	-0.043		0.026	-1.671
	site 10	0.040		0.024	1.672
	site 11	0.027		0.047	0.564
	site 12	-0.013		0.040	-0.324
	site 13	-0.002		0.040	-0.057
	site 14	0.002		0.039	0.051
	site 15	0.006		0.067	0.096
	site 16	-0.017		0.028	-0.598
	site 18	0.051		0.057	0.903
	site 20	0.034		0.059	0.575
	site 21	-0.032		0.030	-1.074
	site 22	0.052		0.078	0.667
	sMRI volume	0.011		0.007	1.592

*** p < .001, ** p < .01, * p < .05

Figure A.22: The results of the analysis of the influence of race and ethnicity.

Age (mother) young, UPPS-P total

R squared = 0.04 — N = 4726

		Coefficient	SE	t-value
	(Intercept)	46.895 ***	4.866	9.638
Prenatal	Nicotine	0.082	0.116	0.706
	Alcohol	0.319 **	0.119	2.679
	Nicotine x Alcohol	-0.223 **	0.083	-2.682
Lifetime Drug Use	Alcohol	-0.096	0.319	-0.300
	Cigarette	4.219 **	1.283	3.288
	E-cigarette	0.472	3.283	0.144
	Cigar	3.035	3.550	0.855
	Hookah	4.790	2.674	1.791
	Chew (smokeless tobacco)	0.628	4.283	0.147
	Pipes	-1.442	2.622	-0.550
	Blunt	-92.212	153.922	-0.599
	Edible(marijuana in food)	2.067	8.800	0.235
	Cathinones (bath salts)	3.597	7.678	0.469
	Inhalant	3.786	7.726	0.490
	Other	-0.370	0.216	-1.713
	Age	-0.019	0.015	-1.281
Sex	Female	-2.560 ***	0.257	-9.962
Race	Black	-0.222	0.412	-0.538
	Hispanic	-0.597	0.372	-1.603
	Asian	-3.449 **	1.063	-3.245
	Other	0.406	0.408	0.995
Parental Education	4th grade	2.079	6.274	0.331
	6th grade	-3.065	4.723	-0.649
	7th grade	-1.565	5.626	-0.278
	8th grade	-2.080	4.754	-0.438
	9th grade	-3.450	4.554	-0.758
	10th grade	-3.101	4.569	-0.679
	11th grade	-2.911	4.504	-0.646
	12th grade	-2.086	4.525	-0.461
	High school graduate	-2.569	4.451	-0.577
	GED or dquivalend Diploma	-1.938	4.493	-0.431
	Some college	-2.986	4.448	-0.671
	Associate degree: Occupational	-2.889	4.455	-0.649
	Associate degree: Academic Program	-2.512	4.462	-0.563
	Bachelor's degree	-2.453	4.450	-0.551
	Master's degree	-3.072	4.456	-0.689
	Professional School degree	-1.819	4.532	-0.401
	Doctoral degree	-2.853	4.526	-0.630
Household Income	$5,000 - $11,999	0.082	0.713	0.115
	$12,000 - $15,999	-0.661	0.835	-0.792
	$16,000 - $24,999	-0.406	0.692	-0.587
	$25,000 - 34,999	0.732	0.663	1.105
	$35,000 - $49,999	0.211	0.657	0.322
	$50,000 - $74,999	0.020	0.643	0.031
	$75,000 - 99,999	-1.139	0.677	-1.682
	$100,000- $199,999	-1.358 *	0.678	-2.004
	$200,000 and greater	-1.409	0.823	-1.711
Parent Marriage	Widowed	-0.358	1.464	-0.244
	Divorced	0.457	0.429	1.067
	Separated	-1.299 *	0.606	-2.144
	Never married	-0.231	0.422	-0.548
	Living with partner	0.522	0.482	1.083
Research Site	site 2	0.110	0.899	0.122
	site 3	-0.015	0.813	-0.018
	site 4	0.325	0.810	0.401
	site 5	2.354 *	0.944	2.493
	site 6	1.442	0.885	1.629
	site 7	3.023 **	0.978	3.092
	site 8	0.420	1.262	0.333
	site 9	0.581	0.931	0.624
	site 10	1.580	0.810	1.950
	site 11	0.222	0.885	0.250
	site 12	1.553	0.878	1.769
	site 13	-0.098	0.845	-0.116
	site 14	0.721	0.922	0.782
	site 15	1.651	0.910	1.815
	site 16	0.350	0.787	0.445
	site 17	2.263 *	0.924	2.450
	site 18	2.049 *	0.999	2.051
	site 19	0.533	0.876	0.608
	site 20	2.048 *	0.843	2.429
	site 21	1.428	0.878	1.627
	site 22	0.968	2.653	0.365
	sMRI volume	-0.286	0.147	-1.946

*** p < .001, ** p < .01, * p < .05

Figure A.23: The results of the analysis on the influence of age of mothers when giving birth to the child. The group included mothers aged younger than 50 percentile of the range of ages.

Age young, SST correct stop vs incorrect stop, left rostral ACC N = 2782

		Coefficient	SE	t-value
	(Intercept)	-0.297	0.268	-1.111
Prenatal	Nicotine	0.002	0.005	0.342
	Alcohol	0.013 *	0.005	2.482
	Nicotine x Alcohol	-0.012 *	0.006	-2.126
Lifetime Drug Use	Alcohol	0.391 **	0.141	2.767
	Cigarette	-0.009	0.042	-0.213
	E-cigarette	0.290	0.251	1.155
	Cigar	-0.047	0.131	-0.357
	Hookah	-0.008	0.090	-0.088
	Chew (smokeless tobacco)	0.060	0.141	0.424
	Pipes	0.007	0.086	0.081
	Edible(marijuana in food)	-0.145	0.288	-0.502
	Inhalant	0.129	0.253	0.508
Age	Age	0.000	0.001	0.351
Sex	Female	0.024 *	0.011	2.229
Race	Black	0.024	0.018	1.284
	Hispanic	0.000	0.016	-0.012
	Asian	0.047	0.046	1.019
	Other	-0.021	0.018	-1.171
Parental Education	4th grade	0.128	0.358	0.358
	6th grade	0.109	0.265	0.411
	7th grade	0.166	0.356	0.467
	8th grade	0.129	0.263	0.490
	9th grade	0.254	0.255	0.996
	10th grade	0.213	0.255	0.838
	11th grade	0.272	0.254	1.074
	12th grade	0.308	0.254	1.211
	High school graduate	0.239	0.251	0.953
	GED or dquivalend Diploma	0.290	0.252	1.151
	Some college	0.236	0.251	0.943
	Associate degree: Occupational	0.233	0.251	0.928
	Associate degree: Academic Program	0.250	0.251	0.993
	Bachelor's degree	0.232	0.251	0.925
	Master's degree	0.239	0.251	0.950
	Professional School degree	0.241	0.253	0.952
	Doctoral degree	0.127	0.254	0.500
Household Income	$5,000 - $11,999	-0.015	0.035	-0.441
	$12,000 - $15,999	0.034	0.038	0.893
	$16,000 - $24,999	-0.037	0.033	-1.119
	$25,000 - 34,999	0.025	0.031	0.792
	$35,000 - $49,999	0.018	0.031	0.588
	$50,000 - $74,999	0.013	0.031	0.408
	$75,000 - 99,999	0.025	0.032	0.785
	$100,000- $199,999	0.022	0.032	0.687
	$200,000 and greater	0.041	0.037	1.112
Parent Marriage	Widowed	-0.118	0.067	-1.763
	Divorced	-0.010	0.018	-0.565
	Separated	-0.001	0.026	-0.041
	Never married	0.003	0.019	0.165
	Living with partner	0.025	0.022	1.169
Research Site	site 3	0.025	0.029	0.878
	site 4	0.026	0.029	0.905
	site 5	0.004	0.032	0.120
	site 6	0.031	0.029	1.053
	site 7	0.005	0.035	0.137
	site 8	0.010	0.050	0.205
	site 9	0.004	0.033	0.129
	site 10	0.028	0.031	0.926
	site 11	0.017	0.031	0.562
	site 12	-0.028	0.030	-0.944
	site 13	0.026	0.030	0.861
	site 14	0.014	0.030	0.456
	site 15	-0.007	0.033	-0.208
	site 16	0.018	0.024	0.768
	site 18	0.036	0.037	0.979
	site 20	0.002	0.027	0.062
	site 21	-0.003	0.031	-0.114
	site 22	0.011	0.128	0.086
	sMRI volume	0.010	0.006	1.645

*** p < .001, ** p < .01, * p < .05

Age young, MID reward anticipation, left accumbens area N = 2995

		Coefficient	SE	t-value
	(Intercept)	0.302	0.231	1.303
Prenatal	Nicotine	-0.001	0.006	-0.161
	Alcohol	-0.002	0.006	-0.261
	Nicotine x Alcohol	-0.013 ***	0.004	-3.306
Lifetime Drug Use	Alcohol	0.080	0.145	0.551
	Cigarette	0.013	0.049	0.258
	E-cigarette	-0.251 *	0.127	-1.981
	Cigar	-0.063	0.150	-0.420
	Hookah	-0.067	0.103	-0.653
	Chew (smokeless tobacco)	0.241	0.172	1.400
	Pipes	-0.021	0.102	-0.206
	Inhalant	0.410	0.297	1.379
Age	Age	0.000	0.001	0.686
Sex	Female	0.002	0.012	0.125
Race	Black	0.015	0.021	0.719
	Hispanic	-0.009	0.017	-0.495
	Asian	-0.040	0.051	-0.786
	Other	0.017	0.020	0.842
Parental Education	4th grade	-0.260	0.363	-0.716
	6th grade	-0.312	0.227	-1.375
	7th grade	-0.514	0.361	-1.426
	8th grade	-0.245	0.230	-1.066
	9th grade	-0.312	0.217	-1.437
	10th grade	-0.232	0.214	-1.082
	11th grade	-0.264	0.212	-1.246
	12th grade	-0.172	0.213	-0.808
	High school graduate	-0.264	0.209	-1.265
	GED or dquivalend Diploma	-0.286	0.211	-1.355
	Some college	-0.249	0.208	-1.197
	Associate degree: Occupational	-0.236	0.209	-1.132
	Associate degree: Academic Program	-0.269	0.209	-1.284
	Bachelor's degree	-0.233	0.209	-1.119
	Master's degree	-0.209	0.209	-0.999
	Professional School degree	-0.217	0.212	-1.022
	Doctoral degree	-0.245	0.213	-1.150
Household Income	$5,000 - $11,999	-0.059	0.038	-1.556
	$12,000 - $15,999	-0.120 **	0.043	-2.801
	$16,000 - $24,999	-0.026	0.037	-0.722
	$25,000 - 34,999	-0.057	0.035	-1.637
	$35,000 - $49,999	-0.051	0.035	-1.486
	$50,000 - $74,999	-0.078 *	0.034	-2.294
	$75,000 - 99,999	-0.057	0.035	-1.594
	$100,000- $199,999	-0.066	0.035	-1.868
	$200,000 and greater	-0.062	0.042	-1.468
Parent Marriage	Widowed	-0.008	0.072	-0.106
	Divorced	0.025	0.021	1.154
	Separated	-0.038	0.029	-1.306
	Never married	-0.030	0.022	-1.399
	Living with partner	-0.031	0.024	-1.280
Research Site	site 3	0.008	0.033	0.252
	site 4	0.013	0.034	0.373
	site 5	-0.026	0.037	-0.714
	site 6	0.019	0.033	0.560
	site 7	0.011	0.039	0.268
	site 8	-0.066	0.056	-1.196
	site 9	-0.003	0.037	-0.079
	site 10	0.006	0.035	0.165
	site 11	0.009	0.035	0.267
	site 12	-0.026	0.033	-0.790
	site 13	-0.021	0.034	-0.632
	site 14	0.020	0.034	0.589
	site 15	0.058	0.037	1.572
	site 16	0.021	0.028	0.767
	site 18	0.042	0.042	0.984
	site 20	0.000	0.031	-0.007
	site 21	-0.005	0.035	-0.137
	site 22	-0.031	0.135	-0.232
	sMRI volume	-0.007	0.007	-1.033

*** p < .001, ** p < .01, * p < .05

Figure A.24: The results of the analysis on the influence of age of mothers when giving birth to the child. The group included mothers aged younger than 50 percentile of the range of ages.

Age old, SST correct stop vs correct go, right pars opercularis				N = 2509
		Coefficient	SE	t-value
	(Intercept)	0.131	0.254	0.518
Prenatal	Nicotine	0.003	0.004	0.804
	Alcohol	-0.010 *	0.005	-2.086
	Nicotine x Alcohol	-0.001	0.009	-0.088
Lifetime Drug Use	Alcohol	-0.031	0.053	-0.577
	E-cigarette	0.012	0.012	1.016
	Cigar	-0.186	1.704	-0.109
	Hookah	0.005	0.172	0.029
	Pills of prescription pain relievers	-0.079	0.171	-0.460
	Age	0.000	0.000	0.466
Sex	Female	0.013	0.008	1.593
Race	Black	0.007	0.017	0.391
	Hispanic	-0.008	0.012	-0.692
	Asian	0.020	0.025	0.811
	Other	-0.019	0.012	-1.569
Parental Education	3th grade	0.056	0.243	0.230
	6th grade	0.075	0.185	0.405
	7th grade	0.179	0.210	0.852
	8th grade	0.156	0.211	0.740
	9th grade	0.008	0.179	0.043
	10th grade	0.113	0.184	0.614
	11th grade	0.058	0.183	0.314
	12th grade	0.012	0.179	0.065
	High school graduate	0.117	0.173	0.677
	GED or dquivalend Diploma	0.007	0.177	0.042
	Some college	0.090	0.173	0.521
	Associate degree: Occupational	0.072	0.173	0.415
	Associate degree: Academic Program	0.077	0.173	0.443
	Bachelor's degree	0.083	0.173	0.482
	Master's degree	0.086	0.173	0.496
	Professional School degree	0.055	0.173	0.320
	Doctoral degree	0.088	0.173	0.511
Household Income	$5,000 - $11,999	-0.077	0.050	-1.523
	$12,000 - $15,999	-0.002	0.048	-0.049
	$16,000 - $24,999	-0.031	0.046	-0.670
	$25,000 - 34,999	-0.032	0.044	-0.731
	$35,000 - $49,999	-0.044	0.042	-1.047
	$50,000 - $74,999	-0.022	0.041	-0.529
	$75,000 - 99,999	-0.017	0.041	-0.412
	$100,000- $199,999	-0.030	0.041	-0.725
	$200,000 and greater	-0.020	0.042	-0.480
Parent Marriage	Widowed	-0.050	0.046	-1.098
	Divorced	0.007	0.013	0.510
	Separated	-0.036	0.022	-1.653
	Never married	0.002	0.021	0.090
	Living with partner	0.024	0.025	0.973
Research Site	site 3	0.007	0.020	0.338
	site 4	-0.091	0.175	-0.522
	site 5	0.003	0.021	0.159
	site 6	-0.008	0.017	-0.448
	site 7	-0.024	0.022	-1.065
	site 8	-0.105	0.173	-0.607
	site 9	-0.021	0.019	-1.074
	site 10	-0.094	0.174	-0.541
	site 11	-0.034	0.026	-1.334
	site 12	-0.013	0.019	-0.696
	site 13	-0.158	0.174	-0.905
	site 14	-0.014	0.016	-0.882
	site 15	0.060 *	0.030	2.025
	site 16	0.007	0.016	0.419
	site 18	-0.147	0.174	-0.844
	site 20	-0.026	0.018	-1.460
	site 21	-0.003	0.017	-0.156
	site 22	-0.154	0.179	-0.856
	sMRI volume	0.001	0.005	0.321
MRI machine	Siemens	-0.107	0.173	-0.618

*** p <.001, ** p <.01, * p <.05

Figure A.25: The results of the analysis on the influence of age of mothers when giving birth to the child. The group included mothers aged older than 50 percentile of the range of ages.

Age old, SST correct stop vs incorrect stop, right pars triagularis			N = 2508
	Coefficient	SE	t-value
(Intercept)	0.422	0.355	1.188

		Coefficient	SE	t-value
	(Intercept)	0.422	0.355	1.188
Prenatal	Nicotine	0.000	0.006	-0.079
	Alcohol	-0.017 *	0.007	-2.528
	Nicotine x Alcohol	-0.006	0.013	-0.467
Lifetime Drug Use	Alcohol	-0.027	0.074	-0.362
	E-cigarette	-0.003	0.016	-0.201
	Cigar	-1.847	2.385	-0.775
	Hookah	-0.063	0.241	-0.261
	Pills of prescription pain relievers	-0.023	0.240	-0.097
	Age	0.000	0.001	-0.010
Sex	Female	-0.003	0.011	-0.236
Race	Black	0.045	0.024	1.840
	Hispanic	-0.023	0.017	-1.382
	Asian	0.023	0.035	0.665
	Other	-0.009	0.017	-0.515
Parental Education	3th grade	-0.360	0.341	-1.057
	6th grade	-0.133	0.259	-0.513
	7th grade	-0.157	0.294	-0.533
	8th grade	-0.186	0.296	-0.630
	9th grade	-0.156	0.251	-0.622
	10th grade	-0.111	0.258	-0.430
	11th grade	-0.204	0.256	-0.797
	12th grade	0.005	0.251	0.021
	High school graduate	-0.128	0.243	-0.528
	GED or dquivalend Diploma	-0.144	0.248	-0.583
	Some college	-0.155	0.242	-0.640
	Associate degree: Occupational	-0.128	0.242	-0.529
	Associate degree: Academic Program	-0.135	0.243	-0.557
	Bachelor's degree	-0.147	0.242	-0.608
	Master's degree	-0.153	0.242	-0.633
	Professional School degree	-0.156	0.243	-0.641
	Doctoral degree	-0.183	0.243	-0.755
Household Income	$5,000 - $11,999	-0.066	0.071	-0.928
	$12,000 - $15,999	0.024	0.068	0.351
	$16,000 - $24,999	-0.039	0.064	-0.609
	$25,000 - 34,999	-0.003	0.061	-0.043
	$35,000 - $49,999	0.033	0.059	0.559
	$50,000 - $74,999	0.029	0.058	0.501
	$75,000 - 99,999	0.028	0.058	0.488
	$100,000- $199,999	0.024	0.058	0.423
	$200,000 and greater	0.028	0.059	0.479
Parent Marriage	Widowed	-0.008	0.064	-0.129
	Divorced	0.013	0.019	0.689
	Separated	-0.008	0.031	-0.267
	Never married	-0.018	0.029	-0.620
	Living with partner	0.095 **	0.035	2.728
Research Site	site 3	0.028	0.027	1.004
	site 4	-0.244	0.245	-0.996
	site 5	-0.007	0.030	-0.248
	site 6	-0.009	0.024	-0.377
	site 7	-0.008	0.031	-0.258
	site 8	-0.277	0.243	-1.140
	site 9	-0.047	0.027	-1.717
	site 10	-0.240	0.244	-0.983
	site 11	0.028	0.036	0.770
	site 12	-0.033	0.026	-1.277
	site 13	-0.297	0.244	-1.219
	site 14	0.027	0.022	1.220
	site 15	0.047	0.042	1.140
	site 16	0.015	0.022	0.676
	site 18	-0.245	0.244	-1.001
	site 20	0.002	0.025	0.066
	site 21	-0.001	0.024	-0.058
	site 22	-0.183	0.251	-0.729
	sMRI volume	0.001	0.006	0.108
MRI machine	Siemens	-0.290	0.242	-1.196

*** p < .001, ** p < .01, * p < .05

Age old, SST correct stop vs incorrect stop, left caudal ACC			N = 2509

		Coefficient	SE	t-value
	(Intercept)	0.055	0.202	0.273
Prenatal	Nicotine	0.000	0.004	-0.091
	Alcohol	-0.008	0.005	-1.585
	Nicotine x Alcohol	0.004 ***	0.001	5.185
Lifetime Drug Use	Alcohol	-0.037	0.057	-0.650
	Cigarette	0.096	0.196	0.490
	E-cigarette	-0.001	0.004	-0.225
	Cigar	13.772	18.749	0.735
	Hookah	-0.044	0.187	-0.233
	Pills of prescription pain relievers	0.039	0.186	0.207
	Age	0.000	0.001	-0.938
Sex	Female	-0.001	0.009	-0.126
Race	Black	-0.001	0.019	-0.042
	Hispanic	-0.007	0.013	-0.518
	Asian	-0.002	0.027	-0.075
	Other	-0.006	0.013	-0.427
Parental Education	3th grade	-0.066	0.264	-0.251
	6th grade	0.057	0.201	0.285
	7th grade	0.067	0.228	0.292
	8th grade	-0.062	0.229	-0.269
	9th grade	-0.016	0.194	-0.081
	10th grade	0.033	0.199	0.165
	11th grade	-0.018	0.198	-0.090
	12th grade	0.095	0.194	0.490
	High school graduate	0.002	0.188	0.009
	GED or dquivalend Diploma	0.051	0.192	0.268
	Some college	0.011	0.187	0.059
	Associate degree: Occupational	-0.009	0.188	-0.049
	Associate degree: Academic Program	-0.006	0.188	-0.030
	Bachelor's degree	0.009	0.187	0.048
	Master's degree	-0.001	0.187	-0.007
	Professional School degree	0.002	0.188	0.009
	Doctoral degree	-0.025	0.188	-0.132
Household Income	$5,000 - $11,999	-0.036	0.055	-0.653
	$12,000 - $15,999	0.019	0.053	0.369
	$16,000 - $24,999	-0.026	0.050	-0.517
	$25,000 - 34,999	-0.018	0.048	-0.372
	$35,000 - $49,999	0.028	0.046	0.613
	$50,000 - $74,999	-0.025	0.045	-0.561
	$75,000 - 99,999	-0.012	0.045	-0.263
	$100,000- $199,999	-0.012	0.045	-0.269
	$200,000 and greater	-0.018	0.045	-0.397
Parent Marriage	Widowed	-0.018	0.049	-0.360
	Divorced	-0.017	0.014	-1.167
	Separated	-0.034	0.024	-1.450
	Never married	-0.010	0.023	-0.462
	Living with partner	0.015	0.027	0.560
Research Site	site 3	0.003	0.021	0.160
	site 4	0.042	0.027	1.590
	site 5	-0.030	0.023	-1.314
	site 6	0.005	0.019	0.256
	site 7	0.001	0.024	0.047
	site 8	-0.039	0.024	-1.637
	site 9	0.000	0.021	0.020
	site 10	0.033	0.022	1.524
	site 11	0.013	0.028	0.451
	site 12	-0.016	0.020	-0.797
	site 13	-0.003	0.020	-0.125
	site 14	0.032	0.017	1.840
	site 15	0.070 *	0.032	2.188
	site 16	0.018	0.017	1.070
	site 18	0.024	0.024	1.018
	site 20	-0.008	0.019	-0.434
	site 21	-0.005	0.019	-0.254
	site 22	0.074	0.050	1.478
	sMRI volume	-0.002	0.005	-0.502

*** p < .001, ** p < .01, * p < .05

Figure A.26: The results of the analysis on the influence of age of mothers when giving birth to the child. The group included mothers aged older than 50 percentile of the range of ages.

SUD alcohol 0, MID reward anticipation, left accumbens area — N = 3183

		Coefficient		SE	t-value
	(Intercept)	0.236		0.170	1.391
Prenatal	Nicotine	0.005		0.005	0.883
	Alcohol	-0.001		0.005	-0.246
	Nicotine x Alcohol	-0.013	***	0.003	-4.357
Lifetime Drug Use	Alcohol	0.009		0.085	0.104
	E-cigarette	-0.832	**	0.291	-2.863
	Cigar	-0.027		0.380	-0.071
	Hookah	-0.068		0.095	-0.713
	Chew (smokeless tobacco)	0.331		0.259	1.276
	Pipes	-0.046		0.112	-0.413
	Inhalant	0.360		0.284	1.267
	Age	-0.001		0.001	-1.048
Sex	Female	0.012		0.012	1.064
Race	Black	0.005		0.020	0.266
	Hispanic	-0.015		0.017	-0.894
	Asian	0.007		0.033	0.221
	Other	0.008		0.019	0.440
Parental Education	4th grade	-0.091		0.244	-0.374
	6th grade	-0.157		0.160	-0.984
	7th grade	-0.244		0.244	-1.000
	8th grade	-0.045		0.169	-0.269
	9th grade	-0.038		0.152	-0.250
	10th grade	-0.231		0.156	-1.480
	11th grade	-0.133		0.148	-0.899
	12th grade	0.012		0.147	0.082
	High school graduate	-0.089		0.142	-0.630
	GED or dquivalend Diploma	-0.121		0.145	-0.835
	Some college	-0.091		0.141	-0.648
	Associate degree: Occupational	-0.101		0.142	-0.714
	Associate degree: Academic Program	-0.138		0.143	-0.971
	Bachelor's degree	-0.081		0.141	-0.577
	Master's degree	-0.079		0.141	-0.561
	Professional School degree	-0.062		0.144	-0.432
	Doctoral degree	-0.098		0.143	-0.683
Household Income	$5,000 - $11,999	-0.011		0.039	-0.289
	$12,000 - $15,999	-0.049		0.042	-1.148
	$16,000 - $24,999	0.021		0.039	0.536
	$25,000 - 34,999	-0.038		0.036	-1.044
	$35,000 - $49,999	-0.006		0.036	-0.177
	$50,000 - $74,999	-0.006		0.035	-0.161
	$75,000 - 99,999	-0.015		0.036	-0.420
	$100,000- $199,999	-0.004		0.036	-0.109
	$200,000 and greater	0.010		0.038	0.270
Parent Marriage	Widowed	0.082		0.065	1.268
	Divorced	0.017		0.021	0.786
	Separated	0.045		0.031	1.437
	Never married	0.005		0.023	0.221
	Living with partner	-0.017		0.027	-0.618
Research Site	site 3	-0.004		0.028	-0.136
	site 4	-0.004		0.033	-0.118
	site 5	-0.033		0.033	-0.988
	site 6	0.004		0.030	0.126
	site 7	-0.010		0.034	-0.281
	site 8	0.004		0.037	0.111
	site 9	-0.010		0.031	-0.322
	site 10	-0.029		0.030	-0.964
	site 11	0.008		0.034	0.236
	site 12	-0.053		0.029	-1.849
	site 13	-0.039		0.030	-1.321
	site 14	0.001		0.029	0.026
	site 15	0.030		0.036	0.832
	site 16	0.008		0.024	0.348
	site 18	0.018		0.038	0.486
	site 20	-0.025		0.028	-0.897
	site 21	-0.016		0.028	-0.565
	site 22	0.033		0.084	0.393
	sMRI volume	0.003		0.007	0.517

*** p < .001, ** p < .01, * p < .05

SUD alcohol 0, SST correct stop vs correct go, left caudal ACC — N = 3008

		Coefficient		SE	t-value
	(Intercept)	-0.032		0.126	-0.257
Prenatal	Nicotine	0.002		0.003	0.696
	Alcohol	-0.001		0.003	-0.279
	Nicotine x Alcohol	0.003	*	0.001	2.039
Lifetime Drug Use	Alcohol	-0.004		0.048	-0.082
	E-cigarette	-0.037		0.079	-0.467
	Cigar	0.650		1.578	0.412
	Hookah	-0.054		0.054	-1.010
	Chew (smokeless tobacco)	0.236		0.133	1.770
	Pipes	-0.089		0.061	-1.456
	Inhalant	0.240		0.160	1.496
	Age	0.000		0.000	-0.674
Sex	Female	0.002		0.007	0.297
Race	Black	0.011		0.012	0.953
	Hispanic	-0.014		0.010	-1.466
	Asian	0.013		0.019	0.653
	Other	-0.011		0.011	-0.991
Parental Education	4th grade	0.017		0.160	0.105
	6th grade	0.082		0.123	0.664
	7th grade	0.323	*	0.159	2.028
	8th grade	0.187		0.123	1.518
	9th grade	0.170		0.117	1.447
	10th grade	0.179		0.121	1.478
	11th grade	0.185		0.116	1.595
	12th grade	0.160		0.116	1.379
	High school graduate	0.153		0.113	1.357
	GED or dquivalend Diploma	0.175		0.114	1.533
	Some college	0.130		0.113	1.153
	Associate degree: Occupational	0.151		0.113	1.336
	Associate degree: Academic Program	0.130		0.113	1.148
	Bachelor's degree	0.144		0.113	1.274
	Master's degree	0.134		0.113	1.186
	Professional School degree	0.121		0.114	1.061
	Doctoral degree	0.150		0.114	1.324
Household Income	$5,000 - $11,999	-0.026		0.024	-1.083
	$12,000 - $15,999	-0.020		0.025	-0.802
	$16,000 - $24,999	-0.060	*	0.023	-2.576
	$25,000 - 34,999	0.002		0.022	0.080
	$35,000 - $49,999	-0.002		0.022	-0.087
	$50,000 - $74,999	-0.017		0.021	-0.802
	$75,000 - 99,999	0.002		0.021	0.115
	$100,000- $199,999	-0.015		0.021	-0.726
	$200,000 and greater	-0.011		0.023	-0.482
Parent Marriage	Widowed	-0.011		0.041	-0.276
	Divorced	0.033	**	0.012	2.727
	Separated	-0.029		0.018	-1.593
	Never married	0.024		0.013	1.777
	Living with partner	0.008		0.016	0.481
Research Site	site 3	0.014		0.016	0.845
	site 4	-0.008		0.019	-0.437
	site 5	-0.017		0.019	-0.867
	site 6	-0.015		0.017	-0.883
	site 7	0.010		0.020	0.496
	site 8	0.005		0.022	0.225
	site 9	-0.018		0.018	-1.005
	site 10	0.015		0.018	0.846
	site 11	-0.016		0.020	-0.819
	site 12	-0.028		0.017	-1.665
	site 13	-0.003		0.018	-0.190
	site 14	0.004		0.016	0.248
	site 15	-0.005		0.021	-0.221
	site 16	0.002		0.014	0.163
	site 18	-0.004		0.021	-0.192
	site 20	-0.022		0.016	-1.359
	site 21	0.006		0.016	0.342
	site 22	-0.016		0.047	-0.329
	sMRI volume	-0.002		0.004	-0.505

*** p < .001, ** p < .01, * p < .05

Figure A.27: The results of the analysis on the influence of mental health of biological mothers. The group included mothers who have never had a problem due to alcohol.

SUD alcohol 1, SST correct stop vs correct go, left caudal ACC				N = 2266
		Coefficient	SE	t-value
(Intercept)		-0.107	0.170	-0.633
Prenatal	Nicotine	0.003	0.003	0.736
	Alcohol	-0.003	0.005	-0.620
	Nicotine x Alcohol	0.005 ***	0.001	4.210
Lifetime Drug Use	Alcohol	-0.170	0.092	-1.844
	E-cigarette	0.016	0.011	1.545
	Cigar	5.961	15.873	0.376
	Chew (smokeless tobacco)	0.026	0.160	0.163
	Pills of prescription pain relievers	0.001	0.158	0.004
Age		0.000	0.000	0.310
Sex	Female	0.001	0.008	0.067
Race	Black	0.012	0.015	0.788
	Hispanic	0.013	0.011	1.222
	Asian	0.014	0.050	0.288
	Other	-0.013	0.011	-1.125
Parental Education	6th grade	0.125	0.177	0.706
	7th grade	0.106	0.222	0.476
	8th grade	0.044	0.183	0.241
	9th grade	0.131	0.163	0.806
	10th grade	0.151	0.161	0.935
	11th grade	0.104	0.162	0.642
	12th grade	0.183	0.164	1.118
	High school graduate	0.139	0.159	0.875
	GED or dquivalend Diploma	0.145	0.161	0.899
	Some college	0.146	0.158	0.919
	Associate degree: Occupational	0.128	0.159	0.809
	Associate degree: Academic Program	0.131	0.159	0.826
	Bachelor's degree	0.124	0.159	0.783
	Master's degree	0.127	0.159	0.802
	Professional School degree	0.136	0.160	0.851
	Doctoral degree	0.131	0.160	0.819
Household Income	$5,000 - $11,999	-0.058	0.036	-1.608
	$12,000 - $15,999	0.029	0.037	0.779
	$16,000 - $24,999	0.006	0.032	0.189
	$25,000 - 34,999	0.030	0.030	0.996
	$35,000 - $49,999	0.006	0.030	0.209
	$50,000 - $74,999	0.016	0.029	0.531
	$75,000 - 99,999	0.036	0.030	1.211
	$100,000- $199,999	0.022	0.030	0.732
	$200,000 and greater	0.032	0.031	1.036
Parent Marriage	Widowed	-0.021	0.042	-0.494
	Divorced	-0.011	0.012	-0.889
	Separated	0.009	0.018	0.509
	Never married	0.028	0.016	1.783
	Living with partner	0.003	0.017	0.206
Research Site	site 3	0.010	0.022	0.463
	site 4	0.021	0.019	1.074
	site 5	-0.005	0.020	-0.247
	site 6	0.000	0.017	0.012
	site 7	-0.003	0.022	-0.150
	site 8	-0.016	0.028	-0.585
	site 9	-0.003	0.020	-0.168
	site 10	0.000	0.020	0.004
	site 11	-0.011	0.021	-0.510
	site 12	0.006	0.019	0.288
	site 13	-0.021	0.018	-1.130
	site 14	0.008	0.016	0.514
	site 15	-0.018	0.024	-0.758
	site 16	0.009	0.015	0.578
	site 18	0.008	0.022	0.356
	site 20	0.009	0.017	0.512
	site 21	-0.007	0.019	-0.353
	site 22	0.014	0.061	0.232
sMRI volume		0.005	0.004	1.162

*** $p < .001$, ** $p < .01$, * $p < .05$

Figure A.28: The results of the analysis on the influence of mental health of biological mothers. The group included mothers who have had at least one problem due to alcohol.

SUD drug 0, SST correct stop vs correct go, left caudal ACC			N = 3762
	Coefficient	SE	t-value
(Intercept)	-0.041	0.122	-0.338

Prenatal			
Nicotine	0.001	0.003	0.535
Alcohol	-0.002	0.003	-0.901
Nicotine x Alcohol	0.004 *	0.002	2.062

Lifetime Drug Use			
Alcohol	-0.001	0.047	-0.028
E-cigarette	-0.043	0.078	-0.546
Cigar	0.570	1.552	0.367
Hookah	-0.045	0.053	-0.850
Chew (smokeless tobacco)	0.242	0.132	1.840
Pipes	-0.084	0.060	-1.397
Edible(marijuana in food)	-0.208	0.205	-1.012
Inhalant	0.191	0.158	1.205
Pills of prescription pain relievers	0.030	0.156	0.193
Age	0.000	0.000	-0.606

Sex			
Female	0.005	0.006	0.795

Race			
Black	0.019	0.011	1.753
Hispanic	-0.006	0.009	-0.740
Asian	0.015	0.018	0.843
Other	-0.004	0.009	-0.435

Parental Education			
4th grade	0.000	0.158	-0.003
6th grade	0.073	0.120	0.607
7th grade	0.242	0.143	1.688
8th grade	0.219	0.126	1.737
9th grade	0.138	0.116	1.183
10th grade	0.135	0.116	1.167
11th grade	0.177	0.115	1.543
12th grade	0.166	0.114	1.458
High school graduate	0.136	0.112	1.222
GED or dquivalend Diploma	0.168	0.113	1.489
Some college	0.120	0.111	1.082
Associate degree: Occupational	0.138	0.112	1.234
Associate degree: Academic Program	0.124	0.112	1.106
Bachelor's degree	0.125	0.111	1.124
Master's degree	0.116	0.111	1.039
Professional School degree	0.112	0.112	1.001
Doctoral degree	0.130	0.112	1.160

Household Income			
$5,000 - $11,999	-0.018	0.023	-0.762
$12,000 - $15,999	-0.017	0.025	-0.664
$16,000 - $24,999	-0.022	0.022	-0.978
$25,000 - 34,999	-0.004	0.021	-0.169
$35,000 - $49,999	0.001	0.020	0.050
$50,000 - $74,999	-0.012	0.020	-0.603
$75,000 - 99,999	0.009	0.020	0.449
$100,000- $199,999	-0.006	0.020	-0.321
$200,000 and greater	0.003	0.021	0.143

Parent Marriage			
Widowed	-0.017	0.032	-0.528
Divorced	0.008	0.011	0.732
Separated	-0.022	0.016	-1.362
Never married	0.013	0.013	1.069
Living with partner	0.012	0.015	0.841

Research Site			
site 3	0.021	0.014	1.479
site 4	0.022	0.017	1.270
site 5	-0.004	0.016	-0.271
site 6	0.004	0.014	0.308
site 7	0.020	0.018	1.125
site 8	0.003	0.019	0.148
site 9	-0.007	0.015	-0.482
site 10	0.020	0.015	1.325
site 11	-0.014	0.017	-0.790
site 12	-0.014	0.015	-0.931
site 13	-0.002	0.015	-0.151
site 14	0.017	0.014	1.285
site 15	0.010	0.018	0.533
site 16	0.010	0.012	0.813
site 18	0.000	0.018	-0.022
site 20	-0.011	0.014	-0.782
site 21	0.019	0.014	1.308
site 22	0.013	0.045	0.295
sMRI volume	0.002	0.003	0.677

*** p < .001, ** p < .01, * p < .05

SUD drug 1, SST correct stop vs correct go, left caudal ACC			N = 1502
	Coefficient	SE	t-value
(Intercept)	-0.078	0.174	-0.447

Prenatal			
Nicotine	0.001	0.004	0.156
Alcohol	-0.005	0.007	-0.689
Nicotine x Alcohol	0.005 ***	0.002	3.553

Lifetime Drug Use			
Alcohol	-0.174	0.094	-1.854
E-cigarette	0.014	0.011	1.358
Cigar	0.197 *	0.093	2.122
Chew (smokeless tobacco)	-0.112	0.159	-0.701
Age	0.000	0.001	0.381

Sex			
Female	0.003	0.009	0.334

Race			
Black	-0.009	0.017	-0.508
Hispanic	-0.005	0.013	-0.385
Asian	-0.116	0.093	-1.247
Other	-0.031 *	0.014	-2.246

Parental Education			
6th grade	0.094	0.193	0.489
8th grade	0.044	0.170	0.258
9th grade	0.157	0.164	0.961
10th grade	0.180	0.164	1.101
11th grade	0.099	0.162	0.607
12th grade	0.114	0.166	0.685
High school graduate	0.145	0.159	0.910
GED or dquivalend Diploma	0.123	0.161	0.765
Some college	0.149	0.158	0.943
Associate degree: Occupational	0.119	0.159	0.747
Associate degree: Academic Program	0.126	0.159	0.793
Bachelor's degree	0.126	0.159	0.794
Master's degree	0.126	0.159	0.797
Professional School degree	0.132	0.161	0.818
Doctoral degree	0.136	0.160	0.847

Household Income			
$5,000 - $11,999	-0.076 *	0.037	-2.059
$12,000 - $15,999	0.011	0.039	0.270
$16,000 - $24,999	-0.024	0.035	-0.682
$25,000 - 34,999	0.033	0.033	1.003
$35,000 - $49,999	-0.006	0.032	-0.200
$50,000 - $74,999	0.012	0.033	0.374
$75,000 - 99,999	0.026	0.033	0.785
$100,000- $199,999	0.003	0.033	0.103
$200,000 and greater	0.003	0.036	0.086

Parent Marriage			
Widowed	-0.016	0.067	-0.243
Divorced	0.007	0.014	0.521
Separated	0.014	0.021	0.641
Never married	0.041 *	0.017	2.339
Living with partner	0.028	0.019	1.529

Research Site			
site 3	-0.006	0.025	-0.245
site 4	-0.020	0.023	-0.894
site 5	-0.030	0.026	-1.136
site 6	-0.038	0.022	-1.749
site 7	-0.035	0.028	-1.254
site 8	0.003	0.038	0.076
site 9	-0.012	0.027	-0.440
site 10	-0.029	0.025	-1.161
site 11	-0.033	0.026	-1.271
site 12	-0.056 *	0.024	-2.310
site 13	-0.031	0.024	-1.317
site 14	-0.031	0.022	-1.407
site 15	-0.058 *	0.029	-2.002
site 16	-0.018	0.019	-0.917
site 18	0.005	0.030	0.154
site 20	-0.008	0.021	-0.379
site 21	-0.021	0.024	-0.842
site 22	-0.048	0.073	-0.667
sMRI volume	0.003	0.005	0.508

*** p < .001, ** p < .01, * p < .05

Figure A.29: The results of the analysis on the influence of mental health of biological mothers. The group included mothers who have never had a problem due to drugs (drug 0). The group included mothers who have had at least one problem due to drugs (drug 1).

Depression0, UPPS-P total
R squared = 0.041   N = 6799

		Coefficient		SE	t-value
	(Intercept)	42.931	***	5.490	7.819
Prenatal	Nicotine	0.110		0.093	1.186
	Alcohol	0.486	***	0.130	3.754
	Nicotine x Alcohol	-0.047	*	0.022	-2.175
Lifetime Drug Use	Alcohol	2.913	*	1.248	2.334
	Cigarette	7.053		7.748	0.910
	E-cigarette	0.418	**	0.160	2.609
	Cigar	-4.372		5.890	-0.742
	Hookah	4.714		2.474	1.905
	Chew (smokeless tobacco)	8.508		5.572	1.527
	Pipes	4.283		7.383	0.580
	Blunt	-72.096		147.988	-0.487
	Edible(marijuana in food)	-5.317		9.255	-0.574
	Inhalant	2.025		7.418	0.273
	Pills of prescription tranquilizers or sedatives	2.926		1.842	1.588
	Pills of prescription pain relievers	9.333		7.369	1.266
	Age	-0.040	**	0.012	-3.264
Sex	Female	-2.554	***	0.206	-12.424
Race	Black	0.055		0.351	0.157
	Hispanic	0.061		0.304	0.201
	Asian	-0.557		0.646	-0.862
	Other	0.649	*	0.323	2.009
Parental Education	2th grade	1.270		9.043	0.140
	3th grade	3.069		6.027	0.509
	4th grade	2.647		6.035	0.439
	5th grade	11.736		7.423	1.581
	6th grade	2.362		5.369	0.440
	7th grade	2.306		5.774	0.399
	8th grade	3.075		5.425	0.567
	9th grade	3.939		5.300	0.743
	10th grade	3.197		5.329	0.600
	11th grade	2.007		5.286	0.380
	12th grade	2.734		5.280	0.518
	High school graduate	3.059		5.235	0.584
	GED or dquivalend Diploma	4.637		5.272	0.880
	Some college	2.565		5.231	0.490
	Associate degree: Occupational	2.679		5.238	0.512
	Associate degree: Academic Program	3.179		5.243	0.606
	Bachelor's degree	2.858		5.232	0.546
	Master's degree	2.262		5.235	0.432
	Professional School degree	3.608		5.256	0.686
	Doctoral degree	2.617		5.254	0.498
Household Income	$5,000 - $11,999	0.150		0.705	0.212
	$12,000 - $15,999	0.034		0.794	0.042
	$16,000 - $24,999	-0.055		0.671	-0.082
	$25,000 - 34,999	0.377		0.649	0.581
	$35,000 - $49,999	0.579		0.629	0.921
	$50,000 - $74,999	0.171		0.614	0.280
	$75,000 - 99,999	-0.339		0.629	-0.538
	$100,000- $199,999	-0.368		0.625	-0.588
	$200,000 and greater	-0.291		0.669	-0.435
Parent Marriage	Widowed	-0.906		1.201	-0.754
	Divorced	0.526		0.350	1.505
	Separated	-0.995		0.531	-1.873
	Never married	0.167		0.387	0.432
	Living with partner	0.074		0.444	0.167
Research Site	site 2	0.712		0.653	1.089
	site 3	-0.240		0.622	-0.387
	site 4	0.161		0.647	0.248
	site 5	2.277	**	0.718	3.169
	site 6	1.979	**	0.679	2.912
	site 7	3.158	***	0.758	4.165
	site 8	1.234		0.754	1.636
	site 9	-0.110		0.676	-0.163
	site 10	1.025		0.620	1.653
	site 11	1.014		0.705	1.438
	site 12	1.147		0.678	1.690
	site 13	0.490		0.645	0.759
	site 14	0.816		0.660	1.237
	site 15	1.155		0.786	1.471
	site 16	0.333		0.608	0.547
	site 17	1.736	**	0.669	2.596
	site 18	1.430		0.755	1.894
	site 19	0.214		0.662	0.324
	site 20	2.034	**	0.642	3.169
	site 21	1.195		0.656	1.820
	site 22	-0.259		1.658	-0.156
	sMRI volume	-0.143		0.119	-1.202

*** p < .001, ** p < .01, * p < .05

Depression1, SST correct stop vs correct go, left caudal ACC   N = 4066

		Coefficient		SE	t-value
	(Intercept)	-0.020		0.234	-0.084
Prenatal	Nicotine	0.002		0.003	0.669
	Alcohol	-0.003		0.004	-0.970
	Nicotine x Alcohol	0.003	***	0.001	4.255
Lifetime Drug Use	Alcohol	-0.042		0.047	-0.894
	E-cigarette	0.019		0.011	1.725
	Cigar	0.702		1.607	0.437
	Hookah	-0.062		0.058	-1.077
	Chew (smokeless tobacco)	0.257		0.145	1.774
	Edible(marijuana in food)	-0.183		0.218	-0.839
	Inhalant	0.222		0.164	1.359
	Pills of prescription pain relievers	0.024		0.162	0.147
	Age	0.000		0.000	-0.051
Sex	Female	0.001		0.006	0.107
Race	Black	0.011		0.011	0.994
	Hispanic	-0.006		0.008	-0.726
	Asian	0.007		0.019	0.352
	Other	-0.011		0.009	-1.191
Parental Education	3th grade	0.004		0.198	0.021
	4th grade	0.037		0.199	0.184
	6th grade	0.067		0.168	0.398
	7th grade	0.262		0.187	1.403
	8th grade	0.149		0.168	0.888
	9th grade	0.160		0.164	0.975
	10th grade	0.167		0.165	1.016
	11th grade	0.146		0.164	0.888
	12th grade	0.138		0.164	0.844
	High school graduate	0.144		0.162	0.891
	GED or dquivalend Diploma	0.168		0.163	1.028
	Some college	0.126		0.162	0.776
	Associate degree: Occupational	0.144		0.162	0.887
	Associate degree: Academic Program	0.121		0.162	0.744
	Bachelor's degree	0.126		0.162	0.777
	Master's degree	0.120		0.162	0.740
	Professional School degree	0.102		0.162	0.628
	Doctoral degree	0.140		0.163	0.859
Household Income	$5,000 - $11,999	-0.053	*	0.024	-2.212
	$12,000 - $15,999	-0.019		0.026	-0.760
	$16,000 - $24,999	-0.042		0.023	-1.866
	$25,000 - 34,999	-0.009		0.021	-0.424
	$35,000 - $49,999	-0.009		0.021	-0.419
	$50,000 - $74,999	-0.014		0.021	-0.672
	$75,000 - 99,999	0.003		0.021	0.146
	$100,000- $199,999	-0.016		0.021	-0.768
	$200,000 and greater	0.001		0.022	0.067
Parent Marriage	Widowed	-0.011		0.037	-0.297
	Divorced	0.018		0.010	1.792
	Separated	-0.010		0.016	-0.652
	Never married	0.006		0.012	0.480
	Living with partner	-0.010		0.014	-0.728
Research Site	site 3	0.016		0.014	1.108
	site 4	-0.029		0.164	-0.177
	site 5	-0.010		0.016	-0.653
	site 6	-0.013		0.014	-0.936
	site 7	0.008		0.017	0.495
	site 8	-0.029		0.163	-0.177
	site 9	-0.007		0.015	-0.467
	site 10	-0.017		0.164	-0.106
	site 11	-0.017		0.017	-0.969
	site 12	-0.022		0.015	-1.474
	site 13	-0.052		0.164	-0.319
	site 14	-0.005		0.013	-0.342
	site 15	-0.008		0.019	-0.440
	site 16	0.002		0.012	0.129
	site 18	-0.035		0.164	-0.216
	site 20	-0.016		0.013	-1.206
	site 21	0.006		0.014	0.433
	site 22	-0.030		0.169	-0.179
	sMRI volume	0.001		0.003	0.206
	MRI machine 3	-0.030		0.163	-0.186

*** p < .001, ** p < .01, * p < .05

Figure A.30: The results of the analysis on the influence of mental health of biological mothers. The group included mothers who have never suffered from depression (depression 0). The group included mothers who have suffered from depression (depression 1).

국문초록

태내 약물 노출은 태아에서 아동, 청소년에 이르기까지 인지신경적 기능에 지속적인 영향을 끼친다. 기존 연구들은 많은 인지신경 기능들 중 다양한 정신 질환과 주요한 관련성을 보이는 보상 처리와 충동성에 주목해왔다. 그러나 기존 연구에는 다음과 같은 한계가 있었다. 먼저 상대적으로 적은 수의 표본을 사용했고, 일상에서는 많은 약물 중독자들이 하나 이상의 약물을 사용하고 있는 데에도 불구하고 다중 약물 사용이 태내 노출에 미치는 영향에 대한 연구는 드물었다. 또한, 인구통계학적 요인이나 생후 환경적 요인이 태내 약물 노출의 영향에 어떻게 관여하는지에 대한 연구가 부족했다. 따라서 본 연구에서는 1) 대규모 표본을 사용해 가장 흔히 사용되는 니코틴과 알코올에 대한 노출 효과를 반복 검증 및 확장하고자 하며, 2) 태내 다중 약물의 보상 처리와 충동성에 대한 상호작용 효과를 검증하고, 3) 인구통계학적 요인이나 생후 환경적 요인이 태내 약물 노출의 영향에 어떻게 관여하는지 살펴보고자 한다. 이러한 목표를 위해 미국의 Adolescent Brain Cognitive Development 연구에서 제공하는 보상 처리와 충동성에 대한 행동 및 뇌 영상 지표를 사용하였다 (N = 10,161). 분석 결과, 태내 니코틴 노출은 반응 억제 동안 또 다른 억제 영역인 하전두회의 과잉 활성과 관련있었고 더불어 반응을 억제하는 동안의 전대상회와 하전두회의 과잉 활성에 대해 니코틴과 알코올이 유의미한 상호작용 효과를 보였다. 이는 태내에서 니코틴과 알코올에 동시 노출되는 것이 가산 효과나 시너지 효과를 내고 있을 가능성을 시사한다. 마지막으로 소수 인종 집단과 나이 많은 어머니로 부터 태어난 자녀의 경우 보상 처리와 반응 억제 중에서 유의미하게 다른 패턴이 나타났다. 종합해보면, 이러한 연구 결과는 태내 다중 약물 노출의 복잡한 효과와 환경적 요인과의 상호작용에 앞으로 더욱 주목해야할 필요성을 제기한다.

주요어: 태내 약물 노출, 다중 약물, 보상처리와 충동성

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감사의 글

석사 졸업 논문을 무사히 마무리할 수 있게 도와주신 많은 분들께 짧은 감사의 인사 드립니다.

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