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Developing a Model to Predict Prevalence of Compulsive Behavior in Individuals with OCD

by

Lindsay D. Fields

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Arts
Department of Mathematics and Statistics
College of Arts and Sciences
University of South Florida

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DEDICATION

To my mother, for showing me how. For making your textbooks my first bedtime stories, for taking me to the library, for helping me with my math homework, even after geometry, for being my first copyeditor, and for coming to every one of my graduations.

We never learned to keep our voices down.
No, we only learned to shout.
So we fight our way in.
And we fight our way out.

-Dashboard Confessional

To Tori, for believing I could. For the late nights and the early mornings, for the summers spent on the other side of the world, for walking the dog when I needed a nap, and for buying me a burrito when I was on my last dime.

I'm a little kid, and so are you.
Don't you go and grow up before I do.

-AJR

To Natalie, for shaming me into doing it right. Just by being there.

Be ready for highs, be ready for lows.
A dream is a dream until you go.
Make some mistakes, don't forget who you are.
Don't reach for the moon, we're going to Mars.

-Judah & the Lion

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LIST OF TERMS

Anion a negatively charged ion

Automata theory a theoretical branch of computer science which considers the logic of computation with respect to simple machines

Automaton an abstract model of a machine which performs computations on an input by moving through a series of states or configurations

Beck Depression Inventory a self-reported test used to rate the severity of depression

Cation a positively charged ion

Clinical Global Impressions Scale a test used to rate severity of symptoms and response to treatment in studies of individuals with mental illnesses

Compulsion a repetitive, ritualistic behavior often used to minimize anxiety

Dendrite a short branched extension of a neuron, along which signals from other cells are received

Dopamine a neurotransmitter which is involved with facilitating the flow of information to the frontal cortex and controlling reward systems within the brain

Dopaminergic reuptake inhibitors a class of drugs that are typically used to treat attention deficit hyperactivity disorder and narcolepsy by increasing the neurotransmission of dopamine

Excoriation an impulse control disorder characterized by repeatedly picking at one's own skin

Functional connectivity the practical relationship between brain regions, regardless of spatial separation

Gamma-aminobutyric acid the most ubiquitous inhibitory neurotransmitter in the adult human brain

Glutamate an excitatory neurotransmitter which is involved in mnemonic functions such as learning and memory formation

In vivo exposure therapy a form of cognitive behavioral therapy that is used to reduce the anxiety associated with phobias

Meta-analysis a statistical analysis that combines the results of multiple scientific studies

Neuron also known as a nerve cell, a cell that receives, processes, and transmits information via electrical and chemical signals

Neurotransmitter a chemical which allows the transmission of signals between neurons across synapses

Noradrenergic reuptake inhibitors a class of drugs that are typically used to treat attention deficit hyperactivity disorder and narcolepsy by increasing the neurotransmission of noradrenaline

Obsession an unwanted and/or intrusive thought or impulse, which can cause a great deal of anxiety when persistent

Selective serotonin reuptake inhibitors a class of drugs that are typically used to treat major depressive disorder and anxiety disorders by increasing the neurotransmission of serotonin

Serotonin a neurotransmitter which is involved in controlling functions such as mood, appetite, and sleep

Structural connectivity the physical relationship between brain regions, in regard to spatial separation

Synapse a region where electrical and chemical signals are transmitted and received

Treatment-naïve having never been treated, either with medication or therapeutically

Trichotillomania an impulse control disorder characterized by repeatedly pulling out one's own hair

Yale-Brown Obsessive Compulsive Scale a test used to rate the severity of OCD symptoms, which measures obsessions separately from compulsions

LIST OF ABBREVIATIONS

ACC	Anterior Cingulate Cortex
APA	American Psychiatric Association
CGI	Clinical Global Impressions
CSTC	Cortico-Striato-Thalamo-Cortical
CT	Computed Tomography
DSM	Diagnostic and Statistical Manual
fMRI	Functional Magnetic Resonance Imaging
GABA	Gamma-Aminobutyric Acid
GPe	Globus Pallidus Externa
GPi	Globus Pallidus Interna
HGF	Hepatocyte Growth Factor
MRI	Magnetic Resonance Imaging
NAA	N-Acetyl-Aspartate
OCD	Obsessive-Compulsive Disorder
OFC	Orbitofrontal Cortex
PET	Positron Emission Tomography
RRNS	Round-Robin Network with Stack
SNr	Substantia Nigra
SSRI	Selective Serotonin Reuptake Inhibitors
STN	Subthalamic Nucleus
VTA	Ventral Tegmental Area
Y-BOCS	Yale-Brown Obsessive Compulsive Scale

ABSTRACT

The most common method of diagnosing Obsessive-Compulsive Disorder is the Yale-Brown Obsessive Compulsive Scale, which measures the severity of symptoms without regard to compulsions. However, this scale is limited to only considering the quantifiable time and energy lost to compulsions. Conversely, current systems of brain imaging arrest mobility and thus make it virtually impossible to observe compulsions at all, focusing instead on neurological responses to external stimuli. There is little research which merges both approaches, to consider the neuro-physiological effects of obsessions as well as the physical response through compulsions. As such, this research is focused on developing a model of compulsivity based upon neurological chemical pathways. The objective is to develop a model which would predict, given a set of environmental parameters, the probability of an individual with OCD performing compulsive behavior and the prevalence of such behavior. By applying this concept to a neural system known as the worry circuit, a computer program was composed and simulations run by this program suggest that the likelihood of compulsive behavior can be predicted using a function of the number of compulsions performed previously. In this model, each neurological agent in the worry circuit, represented by an automaton, has a certain probability of reacting to a stimulus and moving into one of two distinct excited states. Based on the final state of the automaton, the agent will send excitatory or inhibitory signals to surrounding agents, which also have a certain probability of changing states. If the final agent within the cycle shifts into an excited state, the subject will perform a compulsion. These results may be considered preliminary, given the sample size of the case study and the primitive nature of the model.

CHAPTER ONE:
INTRODUCTION

Obsessive-Compulsive Disorder (OCD) is a mental disorder which affects approximately 2.3% of people worldwide at some point in their lives [12]. Individuals with OCD suffer from unwanted and intrusive thoughts or impulses, known as obsessions, which can cause a great deal of anxiety when persistent. Such individuals may then feel compelled to complete repetitive behaviors, or compulsions, to ease their anxiety. Typical compulsions include excessive cleaning of the body or environment, checking, ordering and arranging objects in a precise way, hoarding, and other physical or mental tics. Additionally, many individuals with OCD have tic-related disorders which contribute to compulsive behavior, such as trichotillomania or excoriation: picking of the hair or skin, respectively. Most adults who have OCD are aware that their obsessions and compulsions are irrational, yet feel that they are unable to stop them. People with OCD may attempt to avoid situations which trigger their obsessions, or may self-medicate with drugs or alcohol.

Although it is commonly accepted by mental health experts that obsessions and compulsions are self-perpetuating, there is little research to support this theory. As such, this research proposes that continued ritualistic behavior, as opposed to calming the OCD sufferer, actually serves to amplify anxiety, which in turn incites further rituals. We have designed a model which simulates OCD behavior consistent with this theory for individuals with moderate to severe OCD.

The Problem with Treating OCD as an Anxiety Disorder

The basis for most psychological approaches to OCD is our previous understanding of the neurological markers and effective treatment of anxiety. However, OCD differs significantly from anxiety disorders in the exhibition of compulsive behavior to nullify overwhelming anxiety. For this reason, the fifth edition of the Diagnostic and Statistical Manual (DSM) was updated to separate obsessive-compulsive and related tic disorders from anxiety disorders [1]. Thereby, it is imprudent to continue measuring current methods of treating OCD by their efficacy in treating anxiety disorders.

The most often used method of diagnosing OCD is the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), which measures the severity of obsessive-compulsive symptoms, without considering the content of obsessions or the type of compulsions [13]. However, the scale is limited as it rates symptom severity by the time and energy lost to obsessive and compulsive symptoms, while also relying entirely on self-reporting, which may be inaccurate. On the other hand, current protocols for brain imaging such as magnetic resonance imaging (MRI) and computed tomography (CT) scans arrest mobility and make it virtually impossible to objectively observe physical compulsions while simultaneously scanning neural centers known to induce anxiety.

These limitations influence the health care system by inciting providers to treat only the anxiety aspect of OCD, while perceiving compulsivity as an inherent side effect. As such, it is necessary to develop new methods of treating OCD which are specific to the disorder and allow for improved quality of care.

Chemical Involvement in OCD

Every action relies on neurons within the brain communicating with one another. When a typical neuron is activated by an electrical impulse, it releases a chemical, known as a neurotransmitter, which flows across a synapse and binds to receptors on the receiving neuron's dendrites. At this point, the neurotransmitter causes a new electrical impulse within the receiving dendrite, which may continue the chain [23]. As such, neurotransmitters may be thought of as chemical messages which are transmitted between neurons. Mental illnesses, such as OCD, can occur when this chemical process malfunctions or is interrupted.

Serotonin

Serotonin is a neurotransmitter involved mainly in controlling functions such as mood, appetite, and sleep. Individuals with depression and anxiety have abnormally low levels of serotonin. The belief that serotonin plays a role in OCD originated from the efficacy of selective serotonin reuptake inhibitors (SSRI) as a treatment compared with the inefficacy of noradrenergic and dopaminergic reuptake inhibitors [37], which increase the neurotransmission of noradrenaline and dopamine, respectively. However, the function of the serotonergic system in OCD pathology is unclear, and the data on the matter is inconsistent. It is plausible that SSRI adjust the concentration of serotonin to compensate for another malfunctioning neurotransmitter mechanism.

While SSRI are typically used for depression, the American Psychiatric Association (APA) recommends higher target doses of SSRI to treat OCD than those used to treat major depressive disorder [11], [17]. Patients must also fail to experience improvement on multiple SSRI at the maximum allowable dose for a minimum of

two months before being considered treatment resistant [4]. As such, the 20-40% of OCD patients who do not respond adequately are being treated with significantly higher doses of SSRI for significantly longer periods than other conditions before being offered alternative treatment [37].

Even if patients are not considered to be resistant, they are still being subjected to a lifetime dose of SSRI which is often 300% higher than the temporary dose used for other disorders such as depression, and the average symptom decrease is at most 30-50% [37]. Meta-analysis has shown that these higher doses of SSRI result in greater side-effect burden and lower tolerability in adults [4].

Glutamate

Glutamate is the most ubiquitous excitatory neurotransmitter in the adult human brain and is involved in mnemonic functions such as learning and memory formation [23]. Obtaining an accurate estimate of glutamate concentration from MRI is difficult at the low magnetic field strengths ($\sim$ 1.5 Tesla) used by most MRIs. Furthermore, glutamate and the amino acid glutamine are difficult to differentiate using MRI, due to their low concentrations and similar molecular structures [28]. Therefore, most MRI studies of OCD do not discriminate between glutamate and glutamine, but rather use a composite value *Glx* [41].

Despite this, several glutamate-related genes have been associated with OCD risk [28]. The efficacy of SSRI in treating OCD may be due to the inhibitory impact of serotonin on cortico-striatal glutamate release, as opposed to a causal relationship between serotonin and symptom provocation. Additionally, studies have found that agents which directly reduce glutamate hyperactivity in the central nervous system are effective as therapeutic interventions for OCD [27].

Gamma-Aminobutyric Acid

Gamma-aminobutyric acid (GABA) is the most ubiquitous inhibitory neurotransmitter in the adult human brain, although it is also believed to play an excitatory role in the developing brain [18]. GABA acts by binding to specific transmembrane receptors in both the pre- and post-synapse plasma membranes of neurons. This causes the opening of channels to allow the flow of chloride anions into or potassium cations out of the cell, resulting in a negative change in the transmembrane potential [38].

Previous studies have found altered GABA levels in patients with mood disorders, and low GABA levels are believed to correlate with high obsessive-compulsive symptom severity. Research has shown that hepatocyte growth factor (HGF) increases GABAergic inhibition and that individuals with OCD have significantly less HGF

and decreased plasma levels of GABA [33]. Although the effect of GABA on symptom provocation is generally studied for adults, it has been found that age of OCD onset is negatively correlated with GABA saturation in the medial prefrontal cortex [34].

Dopamine

Dopamine is mainly involved with facilitating the flow of information to the frontal cortex, but it is also linked to reward systems within the brain [23]. As noted previously, a contraindication to the hypothesis of serotonin playing a major role in OCD development is that several patients show no significant symptom improvement on SSRI. However, there is evidence that these patients may benefit from antipsychotics in addition to SSRI [26]. This suggests that dopamine may play a role in OCD, as antipsychotics are known to block receptors in dopamine pathways. Furthermore, several neurological disorders associated with dopaminergic dysfunction, such as Tourette's syndrome, also present with OCD symptoms, particularly in adolescents [26]. This suggests possible common neurobiological mechanisms.

Serotonin tonic inhibition impacts dopamine function in the basal ganglia, which indicates a close relationship between serotonin and dopamine in OCD symptom provocation [15]. MRI studies show decreased dopamine $D_{2/3}$ receptor binding in individuals with OCD, particularly in the ventral striatum [6]. Deep brain stimulation targeting the nucleus accumbens, which is located in the ventral striatum, induces striatal dopamine release, and is associated with significant improvement in obsessive-compulsive symptoms. Furthermore, striatal deep brain stimulation has been known to also increase dopamine in the prefrontal cortex [6].

Brain Circuitry

Compulsive behavior appears to correlate directly with a loss of frontal lobe control. It is commonly accepted that there is cluster of areas in the brain, known as the "worry circuit," which incites pathological compulsions at the expense of impulse control. It is well-established that this circuit includes the orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), thalamus, and the ventral striatum. Rădulescu and Marra propose a network of glutamate excitation, GABA inhibition, and dopamine regulation amongst this area, which also implicates the amygdala and the ventral tegmental area (VTA) [30].

The cortico-striato-thalamo-cortical (CSTC) network has also been implicated in obsessive-compulsive behavior. This includes the globus pallidus interna (GPi), globus pallidus externa (GPe), substantia nigra, and the subthalamic nucleus (STN). Multiple single photon emission computed tomography, positron emission

tomography (PET), and functional magnetic resonance imaging (fMRI) studies have shown increased blood flow and metabolism in this area [27]. A representation of the chemical pathways within the CSTC network is given in Figure 1. The leading theory is that increased activity in the direct pathway over the indirect pathway results in thalamic disinhibition and a self-perpetuating circuit between the thalamus and the OFC [27].

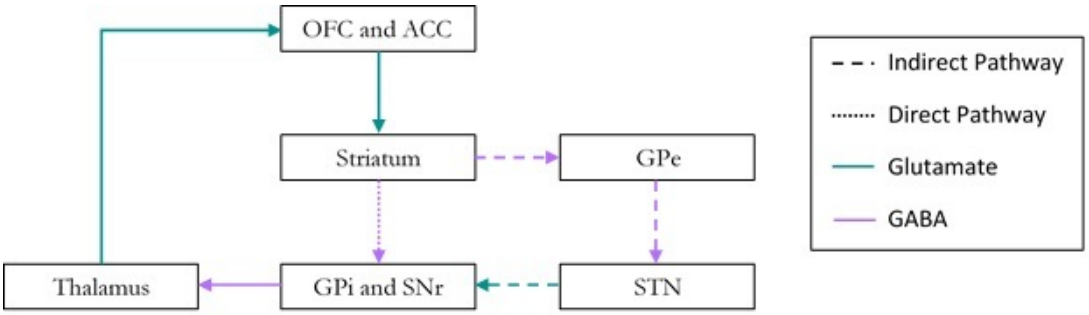

Figure 1: Representation of Cortico-Striato-Thalamo-Cortical Network.*

* In a functional CSTC circuit, glutamatergic signals from the OFC and ACC excite the striatum. Via the direct pathway, the excited striatum sends additional GABA signals to the GPi and substantia nigra (SNr). This inhibits these areas and decreases their GABA output to the thalamus, resulting in greater glutamatergic output from the excited thalamus to the frontal cortex. Via the indirect pathway the striatum instead inhibits the GPe, which decreases its GABA output to the STN. The STN is may then excite the GPi and SNr, which inhibit the thalamus.

For reference purposes, all neural centers discussed have been labelled in Figures 2 and 3.

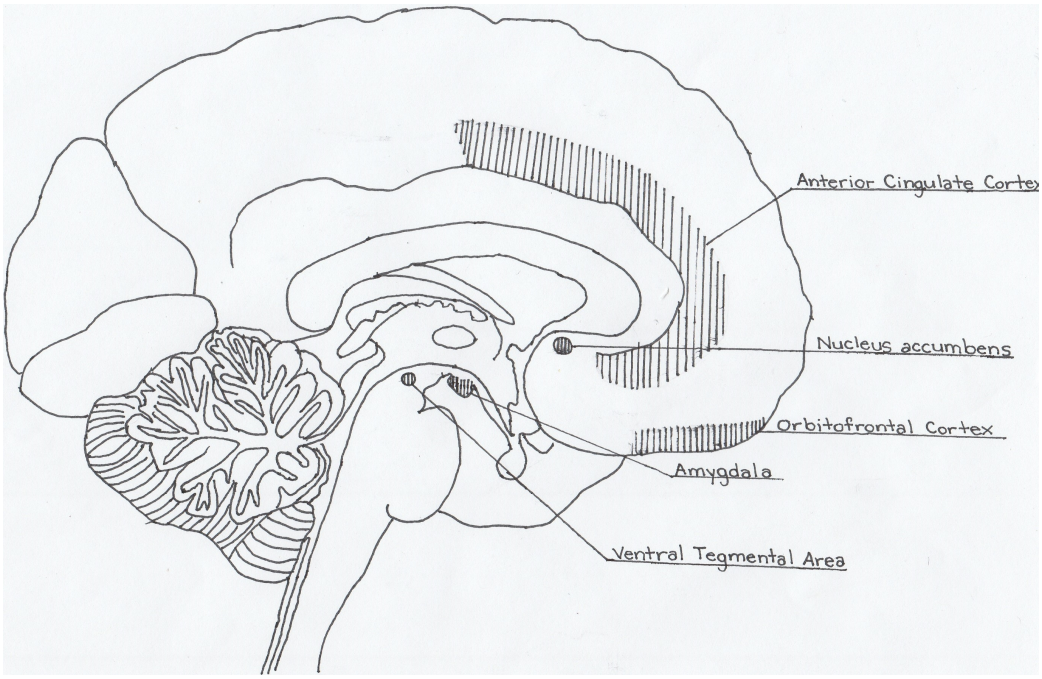

Figure 2: Sagittal Brain Cross-section.

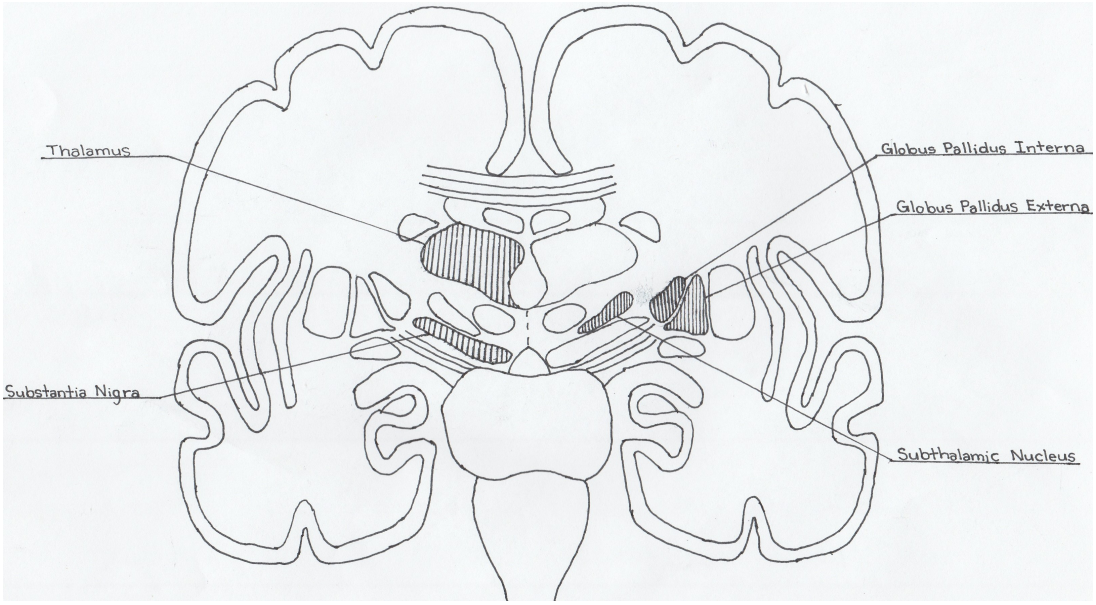

Figure 3: Lateral Brain Cross-section.

Amygdala

The amygdalae are two almond-shaped networks of subnuclei located medially in the temporal lobe. The amygdalae have been shown to perform a role in processing memory, making decisions, and forming emotional responses - such as fear and love conditioning. Patients with OCD display significantly increased functional connectivity of the left amygdala with other centers in the worry circuit in comparison to healthy subjects, although no structural connectivity differences have been observed [32]. Additionally, OCD patients showed a negative correlation between symptom severity and structural integrity of white matter tracts between the amygdalae and other neural centers [32]. These findings suggest that alterations in amygdala structural connectivity could be associated with alterations in functional connectivity elsewhere, and imply that the amygdalae play a relatively strong role in OCD development.

Anterior Cinguate Cortex

The anterior cingulate cortex is active in cognitive processes which involve motivation, regulating emotional responses, and error detection [16]. Hyperactivity within the ACC has an established correlation with OCD symptom presentation [16] and reduced activity in the area has been shown to correlate with greater efficacy of SSRI treatment [9]. However, discrepancies with these findings arise when considering severely drug-resistant OCD; in such cases, it can be assumed that the functional state of the ACC is in constant,

gradual flux throughout OCD development [16]. Furthermore, given that nearly all functions performed by the ACC have contributors in other neural centers, the ACC is considered to have a relatively minor role in OCD development in comparison to other centers in the worry circuit. This theory will be discussed further during the robustness section of this thesis.

Globus Pallidus

The globus pallidus externa is the main regulator of the basal ganglia and uses GABAergic neurons to inhibit the STN, striatum, GPi, and substantia nigra. Via the indirect pathway, the striatum inhibits the GPe, which decreases its inhibition of the STN. The STN may then excite the GPi and substantia nigra, which inhibit the thalamus [25].

The globus pallidus interna is one of the two output nuclei for the basal ganglia and utilizes GABAergic neurons to inhibit the thalamus. Via the direct pathway, the striatum inhibits the GPi, which decreases its inhibition of the thalamus [25]. Where the direct pathway is excitatory, the indirect pathway is inhibitory. Thus, it is believed that excessive activity in the direct pathway results in increased obsessive-compulsive severity.

Studies have found smaller globus pallidus volumes in treatment-naïve children, however no differences have been detected in globus pallidus volumes for adults with OCD compared to healthy controls [19].

Nucleus Accumbens

The nucleus accumbens is part of the ventral striatum in the basal forebrain. The nucleus accumbens plays a major role in processing rewarding and reinforcing stimuli [24]. Patients with OCD have shown decreased reward anticipation in the nucleus accumbens when compared with healthy subjects. Additionally, decreased activity was found to be more pronounced in the nucleus accumbens of patients with contamination fears than in patients with high-risk assessment [7].

Orbitofrontal Cortex

The orbitofrontal cortex directly contributes to reward-based learning and decision making. Recent neurobiological models of OCD predict hyperactivity in circuits involving the OFC [3], and lower activity amongst these circuits is believed to correlate with greater efficacy of SSRI treatment [9]. Such behavior has been recorded during both symptom provocation and resting-state conditions. Additionally, a resting-state fMRI study showed that unmedicated patients with OCD had higher distant and local OFC connectivity than healthy

subjects and significant positive correlations between symptom severity and OFC connectivity [3]. This implies that the OFC plays a major role in OCD development as compared to other centers in the worry circuit.

Substantia Nigra

The substantia nigra is a large cluster of neurons consisting of two parts: the pars reticulata and the pars compacta. The pars compacta synthesizes dopamine and sends it to either the caudate nucleus or the putamen. The dopaminergic cells then inhibit neurons in these areas and influence the GABAergic neuronal output to the pars reticulata, which in turn projects to the thalamus [31].

Subthalamic Nucleus

The subthalamic nucleus is believed to play a major role in decision-making and action-selection [22]. Volumes of the STN have not been assessed in patients with OCD due to its small size, which is exceedingly difficult to measure [19]; however core symptoms of OCD have been attributed to dysfunctional information processing within the STN. Furthermore, for patients with OCD, research has found electrophysiological dysfunctions in the associative and limbic areas of the STN, the latter of which is shown to contribute to checking behavior [22]. Deep brain stimulation of the STN seems to interrupt this disrupted information processing, leading to a normalization of functional connectivity within the CSTC circuit and a reduction in symptoms.

Thalamus

The thalamus is a large area of gray matter that is responsible for relaying sensory and motor signals to the cerebral cortex. Thalamic volume is significantly higher in treatment-naïve patients with OCD than in healthy subjects, and is positively correlated with symptom severity [19]. Furthermore, reduction in the chemical N-acetyl-aspartate (NAA) in the left medial thalamus has been correlated with an increase in OCD symptom severity. However, a significant decrease in the ratios of NAA to choline, creatine, and phosphocreatine has been found in the medial thalamus of patients with OCD, compared to healthy subjects [8]. Given the thalamus' role as the hub for all incoming sensory information, it is believed to play a significant part in OCD development and relaying stimuli to other centers in the worry circuit.

Ventral Tegmental Area

The ventral tegmental area's dopaminergic neurons participate in behavioral disorders, cognition, motivation, and substance abuse. The activity of dopaminergic neurons in the VTA is also linked to reward anticipation. Approximately two thirds of the VTA's neurons are dopaminergic, and most of the remaining neurons are GABAergic. Recently, it has been discovered that the VTA also contains a large number of glutamatergic neurons, as well as that dopaminergic neurons can also release glutamate and GABA [39]. Hence, the VTA outputs a chemically diverse signal.

There is much evidence supporting dopamine's pathology in OCD provocation. Several studies have reported reduced D1 and D2 dopamine receptor binding in the striatum [6], [39]. When dopamine antagonists are used to SSRI, symptom improvement has been observed, especially in the case of patients with comorbid tic disorders [39]. Thus, abnormalities in dopamine modulation via the VTA could be responsible for some of the dysfunction observed in OCD.

CHAPTER TWO:

CASE STUDY

A case study was performed with the purpose of obtaining data from in vivo exposure therapy for individuals with OCD, including the number of compulsive rituals performed at varying levels of exposure severity as well as the amount of time spent performing each ritual. The study was performed over 8 weeks in the OCD clinic at Kyoto Prefectural University of Medicine in Kyoto, Japan. The data obtained through the case study was used to assess the precision of the predictive capabilities of the model. No student, faculty, or other individual affiliated with the University of South Florida was involved in the collection of this data or participant interactions, but only in the analysis and use of the resulting de-identified data.

Inclusion and Exclusion Criteria

The study considered 7 adults with a primary psychiatric diagnosis of OCD as defined by the DSM-V. To be enrolled in the study, participants were required to have physical obsessive-compulsive symptoms of at least moderate severity, defined as at least one observable ritual and a score greater than or equal to 16 on the Y-BOCS. Participants must also have a score greater than or equal to 4 on the Clinical Global Impressions (CGI) scale, which provides a stand-alone assessment of the participant's global mental health functioning prior to the study [5]. Finally, patients were assessed on the Beck Depression Inventory (BDI-II) to determine severity of depressive symptoms, if present, but this score was not used for inclusion purposes. A copy of each of these tests and their rating scales can be found in Appendix B.

Participants were excluded if they had any of the following coexisting disorders: schizophrenia, bipolar disorder, attention deficit/hyperactivity disorder, neurological disorders including Tourette's syndrome, posttraumatic stress disorder, pervasive developmental disorders, or borderline personality disorder. Participants were not excluded from the study on the basis of medication status, but were requested not to alter medication regimens during the study period. Table 1 displays the clinical characteristics of the study participants.

Table 1: Clinical Characteristics of Study Participants.

	# of participants	CGI Score	BDI-II Score	Y-BOCS Score
Contamination	5	5.6 ± 1.14	27.2 ± 12.93	27.6 ± 6.19
Checking	2	6.0 ± 0.00	27.5 ± 13.44	29.0 ± 4.24

Methods

Each participant was seen twice over the course of the study. The first visit consisted of the informed consent procedures and an interview, during which each participant was asked to identify their common triggers and quantify each (on a 1-10 scale) based on severity of anxiety caused. Participants were also asked to identify their common rituals. The second visit consisted of an evaluation of Y-BOCS, CGI, and BDI-II scores and a 90 minute in vivo exposure session.

During the exposure session, each participant was exposed to a mild trigger (identified as 1-3 in inducing anxiety) for 5-30 seconds and asked to freely perform compulsions. The number and length of rituals was noted and the participant was given a ten minute break, during which their blood pressure and heart rate was measured to monitor for negative effects of stress. This process was repeated for moderate (4-7 in inducing anxiety) and severe (8-10) triggers. Although examples can be given of common triggers in each obsessive-compulsive subtype, such as touching a door handle for individuals with contamination fears, it is impossible to generally quantify the severity of such triggers, as the anxiety they induce is unique to each individual.

Due to the use of de-identified data from human subjects, an Institutional Review Board (IRB) exemption was obtained. A letter detailing this exemption can be found in Appendix A.

Results

Given the small sample size for the case study, none of these results may be considered statistically valid, but merely anecdotal. Initially, all data was compiled and considered in aggregate, as seen in Table 2, which shows the means and sample standard deviations. Although this allowed for a more accurate approximation across obsessive-compulsive pathologies, these results were widely varied and difficult to model, due to the heterogeneous nature of OCD. Furthermore, the sample size limited the number of exposures performed at each trigger severity. As such, individual outliers, such as that seen in the duration of rituals at trigger severity 8, had a stronger impact than they would have in a larger sample population.

Table 2: Compulsive Characteristics at Varying Trigger Severities.

Trigger Severity	Number of Compulsions	Duration of Rituals (s)
1	2.00 ± 0.000	26.00 ± 2.828
2	1.00 ± 0.000	22.50 ± 21.920
3	4.50 ± 3.786	15.89 ± 19.311
4	1.33 ± 0.577	38.75 ± 37.358
5	2.00 ± 1.414	9.25 ± 5.315
6	2.50 ± 2.121	38.60 ± 16.607
7	10.00 ± 0.000	3.85 ± 3.431
8	1.00 ± 0.000	171.00 ± 0.000
9	11.00 ± 11.314	6.77 ± 9.056
10	11.33 ± 12.342	29.15 ± 18.746

The data was then compiled to separate contamination from checking pathologies. This allowed for analysis of the model's accuracy, while separating data which may be largely varied and heterogeneous in nature. As seen in Tables 3 and 4, on average, there were fewer compulsions for those with contamination fears, and more time spent per ritual. This is likely due to the higher cost of rituals for contamination versus checking; it takes longer for an individual to satisfactorily complete a decontamination ritual, such as washing their hands, than to complete a cursory check of a lock, for instance. Additionally, decontamination rituals generally take a higher physical toll than checking rituals. For example, excessive hand washing can cause severe dermatitis, while compulsive tooth brushing can lead to torn, bleeding gums and weaken the structural integrity of teeth [14].

Table 3: Compulsive Characteristics for Contamination Pathologies.*

Trigger Severity	Number of Compulsions	Duration of Rituals (s)
1	2.00 ± 0.000	26.00 ± 2.828
2	1.00 ± 0.000	38.00 ± 0.000
3	2.67 ± 1.155	34.13 ± 14.885
4	1.50 ± 0.707	47.67 ± 40.204
5	1.00 ± 0.000	15.00 ± 0.000
6	2.50 ± 2.121	38.60 ± 16.607
7		
8	1.00 ± 0.000	171.00 ± 0.000
9	3.00 ± 0.000	25.00 ± 6.083
10	11.33 ± 12.342	29.15 ± 18.746

* No participants were exposed to a trigger of severity 7.

Table 4: Compulsive Characteristics for Checking Pathologies.*

Trigger Severity	Number of Compulsions	Duration of Rituals (s)
1		
2	1.00 ± 0.000	7.00 ± 0.000
3	10.00 ± 0.000	$1.30 \pm$ †
4	1.00 ± 0.000	12.00 ± 0.000
5	3.00 ± 0.000	7.33 ± 4.509
6		
7	10.00 ± 0.000	3.85 ± 3.431
8		
9	19.00 ± 0.000	3.89 ± 5.237
10		

* No participants were exposed to triggers of severity 1, 6, 8, or 10.
† The rituals at trigger severity 3 were too rapid to be measured individually. Thus standard deviations were not calculated.

Finally, the data was compiled to determine the final number of compulsions performed given each starting value. This data is the closest to that which would be predicted by our model. As seen in Table 5, the rate of increase in the final number of compulsions for contamination pathologies was higher for higher numbers of previous compulsions. However, this behavior was not observed for checking pathologies, perhaps due to the smaller sample size being unable to outweigh outliers as effectively.

Table 5: Compulsive Characteristics at Varying Previous Compulsions.*

Previous Compulsions	Final Compulsions		
	Contamination Pathologies	Checking Pathologies	All Pathologies
0	1.60 ± 0.548	5.50 ± 6.364	2.71 ± 3.251
1	2.00 ± 0.000	2.00 ± 0.000	2.00 ± 0.000
2	4.40 ± 1.517	5.00 ± 0.000	4.50 ± 1.378
3			
4	7.00 ± 0.000		7.00 ± 0.000
5			
6	22.50 ± 12.021		22.50 ± 12.021
7			
8			
9			
10		20.00 ± 0.000	20.00 ± 0.000

* No participants had 3, 5, 7, 8, or 9 previous compulsions.

CHAPTER THREE:
PREDICTIVE MODEL

The model utilized in this research was inspired by automata theory, a simple signaling game, and the Society of Mind metaphor.

Society of Mind

In the late 1960s, Marvin Minsky and Seymour Papert attempted to develop a robot which would build structures using children's blocks. The robot consisted of a computer, a mechanical arm, and a camera. However, it took the designers several years to program hundreds of functions such as Move, See, and Grasp. Thus, Minsky concluded that no single algorithm could solve even the simplest problems. Rather, it required "hundreds of other little programs" [20]. This led him to believe that intelligence was not the product of any simple algorithm for thinking, but of the combined activity of great societies of more specialized cognitive processes.

The Society of Mind model views the human mind as a large society of individually simple processes, known as agents, each specialized to perform a unique function. Each agent is simple by itself, but a combination of several agents can perform complex tasks. These agents are the fundamental entities which form minds and, together, yield the abilities which we attribute to minds. However, different agents can be based on different types of processes with different functions, ways of representing knowledge, and systems for generating results. Thus, we may think of the entire society as being noncooperative [20]. We adopt this metaphor for our model. We will first review some extant models.

Signaling Game

A signaling game is a game with two players, a sender and a receiver. The sender can have one of several types, θ_s, which determines the set of possible messages. The sender's type is private information and is not known by the receiver. The receiver has only a single type, θ_r, known by both players. The game has two steps:

- The sender plays first. They can play one of several actions, called messages.

- The receiver plays second, in response to the sender's message [10].

This theory inspired the method of communication between neural centers for our model.

Automata Theory

Automata theory is a theoretical branch of computer science established in the 20th century, as mathematicians began developing machines which could imitate certain features of humans and complete calculations more quickly and reliably. Automata theory concerns computation by finite discrete machines, called automata. Through automata, computer scientists are able to understand how machines solve problems and compute functions.

An automaton is an abstract model of a machine that performs computations on an input by moving through a series of states. At each point of the computation, a transition function reads the input, one symbol at a time, and determines the next state based on the present symbol and state. As a result, if the computation reaches an accepting state, it accepts that input.

Our model differs from typical deterministic automata, as we include a probability matrix to determine state transitions, define an output alphabet as opposed to an accepting state, and utilize a compulsions counter, designed as a stack.

Probabilistic Automata

Specifically, we are utilizing probabilistic automata. Introduced by Michael Rabin in 1963, a probabilistic automaton is formally defined as a 5-tuple $\langle Q, \Sigma, M, q_0, F\rangle$ where:

- $Q = \{q_0, ..., q_n\}$ is a finite set of states.
- Σ is a finite set called the input alphabet.
- M is a function $M : Q{\times}\Sigma \to [0,1]^{(n+1)\times 1}$ such that, for $(q, \sigma) \in Q{\times}\Sigma$,

$$M(q,\sigma) = \big(p_0(q,\sigma), ..., p_n(q,\sigma)\big), \quad 0 \le p_i(q,\sigma), \quad \sum_i p_i(q,\sigma) = 1,$$

  where $[0,1]$ is the closed unit interval $0 \le x \le 1$, $[0,1]^{n+1}$ is the set of all $n+1$-tuples $(x_0, ..., x_n)$ where $0 \le x_i \le 1$, and $[0,1]^{(n+1)\times 1}$ is the transition probabilities table.
- $q_0 \in Q$ is the initial state.
- $F \subseteq Q$ is the set of accepting states.

When in state q, for any input $\sigma \in \Sigma$, the automaton may enter any one of the states $q_i \in Q$ and the probability of entering q_i is the $(i+1)$st coordinate $p_i(q, \sigma)$ of $M(q, \sigma)$. These transition probabilities $p_i(q, \sigma)$ are independent of time and previous inputs [29].

Note that probabilistic automata accept or reject each input. Our model does not accept or reject inputs, nor contain a set of accepting states. However, we adopt the function M to determine the probability of each automaton shifting states.

Moore Machines

Our model is designed similarly to a network of Moore machines. Developed in 1956 by Edward Moore, a Moore machine is a finite-state machine whose output values are determined solely by its current state. A Moore machine can be formally defined as a 6-tuple $\langle Q, q_0, \Sigma, \Lambda, T, G \rangle$ where:

- $Q = \{q_0, ..., q_n\}$ is a finite set of states.
- $q_0 \in Q$ is the initial state.
- Σ is the input alphabet.
- Λ is the output alphabet.
- T is a transition function $T : Q \times \Sigma \to Q$ mapping a state and the input alphabet to the next state.
- G is an output function $G : Q \to \Lambda$ mapping each state to the output alphabet [21].

Our model differs from a network of Moore machines only by the use of a Rabin-esque probability function M in place of the transition function, T. As such, we deem this a Rabin-Moore automata system. Similar systems were designed by Stark utilizing cellular automata ([35], [36]), however Stark updated random subsets of automata at each time increment, whereas our model updates each automaton individually, thus, consideration must be made for executing order.

Model

Each center within the worry circuit was modeled by an automaton with up to three states: unexcited, excited, or highly excited. These automata communicate with one another through a round robin-style network with a central stack, defined below. At the head of the network is the thalamus which sends a signal around the network until reaching the OFC. The model is designed to predict the final number of compulsions performed in a run of cycles, given the number of compulsions performed previously and the severity of the external trigger. A run terminates when a cycle ends without producing a compulsion.

Network

The communication between the automata in this model is given by a system which we call a Round-Robin Network with Stack (RRNS). We call this a "round-robin" network because each automaton (defined below) is called individually in circular order, and the "stack" refers to an object the automata can read from or write onto. We formally define an RRNS as a 5-tuple $\langle D, \alpha, \Pi, \Sigma, \zeta \rangle$, where:

- $D = \langle V, A \rangle$ is a digraph, with vertices, V, and arcs, A;
- α is a function such that, $\forall v \in V$, $\alpha(v)$ is an automaton defined by a 9-tuple, below;
- Π is the stack alphabet;
- Σ is the communication alphabet;
- ζ, a bijection, $\zeta : \{1, ..., |V|\} \to V$, is the schedule.

We now characterize the automata $\alpha(v), v \in V$.

Automata

For every $v \in V$, let $\text{In}(v) = \{u \in V : \text{arc}(u, v)\}$ and $\text{Out}(v) = \{u \in V : \text{arc}(v, u)\}$. For every automaton, $\alpha(v)$, let $\text{In}_{\alpha(v)} = \{\alpha(u) : u \in \text{In}(v)\}$ and $\text{Out}_{\alpha(v)} = \{\alpha(u) : u \in \text{Out}(v)\}$. We define each $\alpha(v)$, over alphabet Σ, as a 9-tuple $\left\langle Q_{\alpha(v)}, \Theta_{\alpha(v)}, \Lambda_{\alpha(v)}, \gamma, \Pi_{\alpha(v)}, M_{\alpha(v)}, \delta_{\alpha(v)}, q_0, G_{\alpha(v)} \right\rangle$, where:

- $Q_{\alpha(v)} = \{q_0, ..., q_n\}$ is the finite set of states;
- $\Theta_{\alpha(v)} = \{\{(\alpha(u), \alpha(v), \sigma_i) : \alpha(u) \in \text{In}_{\alpha(v)}\} : \forall i, \sigma_i \in \Sigma\}$ is the input alphabet;
- $\Lambda_{\alpha(v)} = \{\{(\alpha(v), \alpha(u), \sigma_o) : \alpha(u) \in \text{Out}_{\alpha(v)}\} : \forall o, \sigma_o \in \Sigma\}$ is the output alphabet;
- $\gamma \in \Pi^*$ is the content of the stack;
- $\Pi_{\alpha(v)} \subseteq \Pi$ is the stack input alphabet. An element HALT is in the stack input alphabet of some automata to end the cycle;
- $M_{\alpha(v)}$ is a function $M_{\alpha(v)} : Q_{\alpha(v)} \times \mathcal{P}(\Theta_{\alpha(v)}) \times \gamma \to [0, 1]^{(n+1)\times 1}$ such that, for $(q, \theta, \gamma) \in Q_{\alpha(v)} \times \mathcal{P}(\Theta_{\alpha(v)}) \times \gamma$,

$$M_{\alpha(v)}(q, \theta, \gamma) = \big(p_0(q, \theta, \gamma), ..., p_n(q, \theta, \gamma)\big), \quad 0 \leq p_i(q, \theta, \gamma), \quad \sum_i p_i(q, \theta, \gamma) = 1,$$

where $[0, 1]^{(n+1)\times 1}$ is the transition probabilities table, $\mathcal{P}(\Theta_{\alpha(v)})$ denotes the power set of $\Theta_{\alpha(v)}$, and $p_i(q, \theta, \gamma)$ is the probability of $\alpha(v)$ shifting to state q_i;

- $\delta_{\alpha(v)}$ is a function, $\delta_{\alpha(v)} : Q_{\alpha(v)} \times \Pi^* \to \Pi^*$, which concatenates the stack with its input $\delta_{\alpha(v)}(q, \gamma) = \gamma + \pi$, where $\pi \in \Pi_{\alpha(v)} \cup \{\varepsilon\}$, ε the empty string;
- $q_0 \in Q$ is the initial state;
- $G_{\alpha(v)}$ is an output function $G_{\alpha(v)} : Q_{\alpha(v)} \to \mathcal{P}(\Lambda_{\alpha(v)})$ mapping each state into the output alphabet.

Schedule and Updates

For a given RRNS, $\mathcal{R}$, with schedule $\zeta : \{1, ..., |\alpha(v)|\} \to \alpha(v)$, let $\alpha_j = \alpha(\zeta(j))$. α_1 contains the initial stack, γ_0, and input alphabet $\Theta_{\alpha_1} = \{\}$. At time t, if α_t is in state q, with stack γ, α_t has $\theta \subseteq \Theta_{\alpha_t} = \{\{(\alpha_k, \alpha_t, \sigma_i) : \alpha_k \in \text{In}_{\alpha_t}, k < t\} : \forall i, \sigma_i \in \Sigma\}$, shifts into state q_i with probability $p_i(q, \theta, \gamma)$, and outputs $G_{\alpha_t}(q_i) \in \Lambda_{\alpha_t} = \{\{(\alpha_t, \alpha_k, \sigma_o) : \alpha_k \in \text{Out}_{\alpha_t}, k > t\} : \forall o, \sigma_o \in \Sigma\}$. If $t \neq t'$, then no change occurs in $\alpha_{t'}$ at time t. The index, $t := t \bmod |\alpha_t| + 1$, updates and the cycle moves to α_{t+1}.

Whenever an automaton α_t adds to the stack (i.e. $\delta_{\alpha_t}(q, \gamma) \neq \gamma$), $\delta_{\alpha_t}(q, \gamma)$ replaces γ as the stack in all automata. This continues until HALT $\in \delta_{\alpha_t}(q, \gamma)$. It is important to note that if every automaton in the network contains an element $\pi \in \Pi_{\alpha(v)}$, $\pi \neq$ HALT, then the network can compute indefinitely.

Operation of Network

Each automaton in the network receives input from the automata which communicate with it from further up the cycle. The automaton then performs a transition function on these inputs to determine its state and sends outputs to the automata it communicates with further down the cycle. As such, inputs move around the cycle in a particular order, and outputs are returned to the starting point via the stack.

Example. We give an example of a RRNS $\langle D, A_i, \{1, \text{HALT}\}, \{-1, 0, 1\}, \zeta\rangle$ with $\zeta : |A_i| \to A_i, i = 1, 2, 3$, a digraph, D, and three automata given below:

$$A_1 = \left\langle \{0,1\}, \{\}, \Lambda_{A_1}, \{\varepsilon\}, \{\}, \left(\tfrac{1}{3}, \tfrac{2}{3}\right), \{\varepsilon\}, 1, \{0 \mapsto 0, 1 \mapsto 1\}\right\rangle,$$
$$\Lambda_{A_1} = \{(A_1, A_2, 0), (A_1, A_2, 1), (A_1, A_3, 0), (A_1, A_3, 1)\};$$

$$A_2 = \left\langle \{0,1\}, \Theta_{A_2}, \Lambda_{A_2}, \{\varepsilon\}, \{\}, \left(\tfrac{2}{3}, \tfrac{1}{3}\right), \{\varepsilon\}, 0, \{0 \mapsto -1, 1 \mapsto 0\}\right\rangle,$$
$$\Theta_{A_2} = \{(A_1, A_2, 0), (A_1, A_2, 1)\}, \Lambda_{A_2} = \{(A_2, A_3, -1), (A_2, A_3, 0)\};$$

$$A_3 = \left\langle \{0,1,2\}, \Theta_{A_3}, \{\}, \{\varepsilon\}, \{1, \text{HALT}\}, \left(\tfrac{2}{5}, \tfrac{2}{5}, \tfrac{1}{5}\right), \{\text{HALT}\}, 0, \{0 \mapsto -1, 1 \mapsto 0, 2 \mapsto 1\}\right\rangle,$$
$$\Theta_{A_3} = \{(A_1, A_3, 0), (A_1, A_3, 1), (A_2, A_3, -1), (A_2, A_3, 0)\}$$

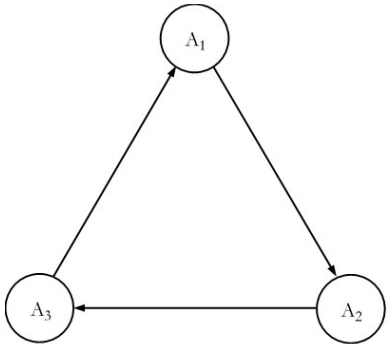

Figure 4: Example Digraph.

It is important to note that G_{A_i} for each A_i outputs the same signal to every $A_j, i \neq j$.

Step 1: A_1 begins in state 1 and stays in state 1, with probability $\frac{2}{3}$, so A_1 outputs $(A_1, A_2, 1), (A_1, A_3, 1)$.

Step 2: A_2 begins in state 0 and shifts to state 1, with probability $\frac{1}{3}$, so A_2 outputs $(A_2, A_3, 0)$.

Step 3: A_3 begins in state 0 and stays in state 0, with probability $\frac{2}{5}$, so A_3 adds HALT to the stack, and the computation ends.

Model Specifics

Our model represents the worry circuit as an RRNS, where each neural center of the worry circuit is represented by an automaton, C, and Θ_C and Λ_C are based on the glutamate, GABA, and dopamine pathways between each center. Figure 5 displays the pathways used for this model as a digraph.

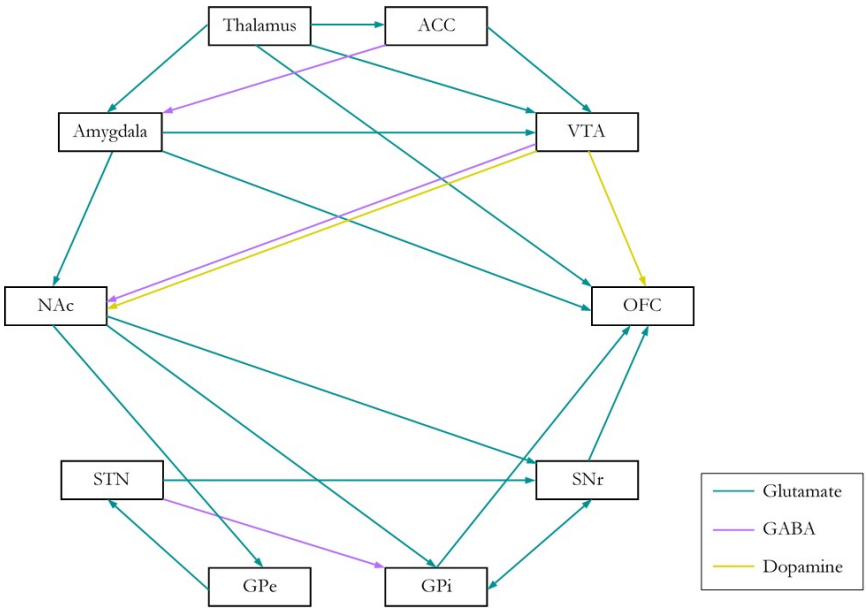

Figure 5: Digraph Representing Round Robin Network.

The content of each automaton in our model is detailed as below.

States. The amygdala and OFC have the set of states, $Q_{\text{Am,OFC}} =$ {unexcited, excited, highly excited}, while the other automata have the set $Q_C =$ {unexcited, excited} for $C \neq$ Am, OFC.

Input Alphabet. The input alphabet for C is the set of messages that can be received by the neural center, C. Each element contains the center which sent the message, c_i, and C, and the excitatory or inhibitory signal, σ, from the sender. Glutamate, being excitatory, provides $\sigma = 1$ or $\sigma = 2$. GABA, being inhibitory, provides $\sigma = -1$. Dopamine can provide either $\sigma = 1$ or $\sigma = -1$ as it is a regulatory chemical. If the center is unexcited $\sigma = 0$.

Output Alphabet. The output alphabet is the set of messages sent by the neural center, C, to all appropriate recipients. Each message contains C, and the center which receives the message, c_o, and the excitatory or inhibitory signal, σ, from the sender. Again, glutamate provides $\sigma = 1$ or $\sigma = 2$, GABA provides $\sigma = -1$, and dopamine provides $\sigma = 1$ or $\sigma = -1$. Whether λ includes a 2 depends upon whether "highly excited" $\in Q$. For example, the message $\lambda = (\text{Am}, \text{Th}, 1)$ is an excitatory signal from the amygdala to the thalamus.

Initial Stack. The initial stack consists of a string of ones, where the cardinality of the stack equals the number of previous compulsions. Furthermore, each cycle's γ equals the previous cycle's δ. As such, δ keeps a running total of the number of compulsions.

Stack Input Alphabet. Because a compulsion is added every time the OFC becomes excited, $\Pi_{\text{OFC}} = \{1, \text{HALT}\}$, and $\Pi_C = \{\}$ for $C \neq$ OFC.

Probability Matrix. Each input is used in a function, $f : \Theta \to \mathbb{Q}$, mapping the input into the closed interval $[-0.02,\ 0.02]$. For example, $f_{\text{Th}} = \begin{cases} 0 & \text{if } \theta = (\text{Am}, \text{Th}, 0) \\ 0.01 & \text{if } \theta = (\text{Am}, \text{Th}, 1) \end{cases}$ provides the thalamus' f-values for inputs from the amygdala. The lower bound for the probability distribution is given by $b = (w \times card(\gamma)) + (10w \times \text{trigger severity}) + \sum f_i$, where w is 0.001 for the centers in the indirect pathway, and 0.002 elsewhere. The trigger severity is a fixed value used in all automata. A probability threshold is given by $t = 15 \sum f_i^+$, where f_i^+ is the positive f-values and the coefficient was obtained by comparing simulated with observed results. The probability value is then randomly chosen via a continuous uniform distribution between b and 1 and, should this value exceed t, the automaton will become excited. Thus, $M(q, \theta, \gamma) = \left(\frac{t-b}{1-b}, \frac{1-t}{1-b}\right)$.

Output Function. The output function is based solely on the state of the automaton. If the automaton is unexcited, it will output either a 0 or a -1 to each of the automata it communicates with. Similarly, an excited automaton will send a 0 or a 1 and a highly excited automaton will send a 0, a 1, or a 2.

Results

Table 6 shows the model's simulations for when no compulsions have been performed previously. A full account of the model's simulations can be found in Table 13 in Appendix C or in Figure 6 below.

Table 6: Simulated Characteristics with No Previous Compulsions.

Trigger Severity	Number of Compulsions
1	1.840 ± 2.3942
2	1.926 ± 2.4051
3	2.130 ± 2.5553
4	2.278 ± 2.8104
5	2.452 ± 2.8245
6	2.701 ± 3.3125
7	3.052 ± 3.7028
8	3.122 ± 3.7007
9	3.689 ± 4.2585
10	4.051 ± 4.7342

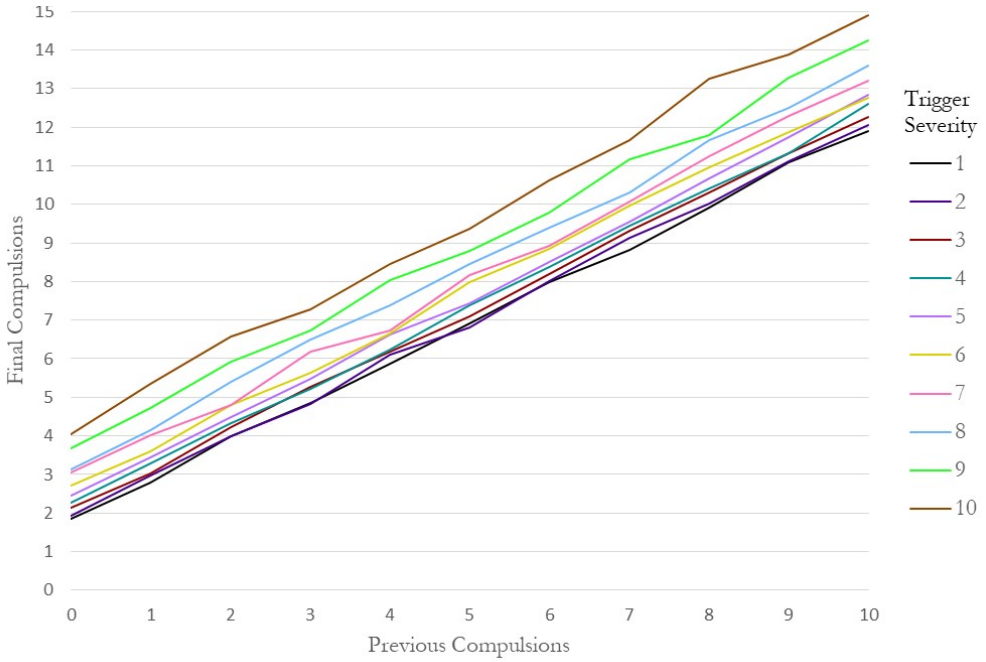

Figure 6: Simulated Characteristics at Varying Previous Compulsions.

Tests for Robustness

Robustness can be roughly defined as the preservation of the accuracy of a program under variations. Minor variations, such as reordering, should not create drastic changes in the accuracy of the program's functionality. However, major changes, such as removing components, should impact accuracy. Given that our model works with very small numbers of compulsions (≤ 15) and a high number of iterations ($= 1000$), we are recognizing 0.140 compulsions as a considerable difference.

Reordering of Automata

Due to the webbed nature of the network, there are multiple orders in which the cycle could execute. This robustness test involves rearranging the variable automata and observing the change in results.

The order used in our model is given by the following rules:

- $\zeta(1) =$ Thalamus;
- $\zeta(2), \zeta(3), \zeta(4) \in \{$ACC, Amygdala, VTA$\}$;
- $\zeta(5) =$ Nucleus accumbens;
- $\zeta(6) =$ GPe;
- $\zeta(7) =$ STN;
- $\zeta(8), \zeta(9) \in \{$Substantia nigra, GPi$\}$;
- $\zeta(10) =$ OFC.

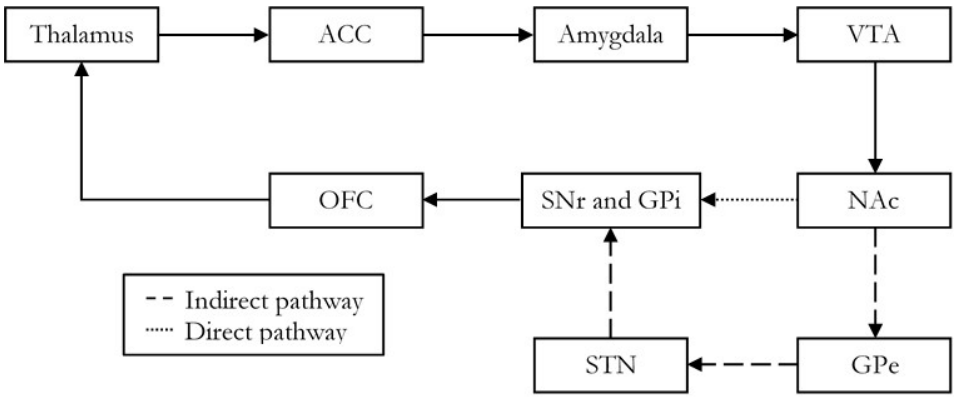

Figure 7: Ordered Representation of Model Brain Circuit.*

* Nodes represent the thalamus, ACC, amygdala, VTA, nucleus accumbens (NAc), GPi, GPe, STN, substantia nigra (SNr), and OFC.

Figure 7 shows the order in which the model calls each automaton. Thus, there are 12 possible cycle options. Table 7 displays all possible options, where Option 1 is the order used in the model.

Table 7: Possible Reorderings of Automata.

Option	Order
1	Th → ACC → Am → VTA → NAc → GPe → STN → SNr → GPi → OFC
2	Th → ACC → Am → VTA → NAc → GPe → STN → GPi → SNr → OFC
3	Th → ACC → VTA → Am → NAc → GPe → STN → SNr → GPi → OFC
4	Th → ACC → VTA → Am → NAc → GPe → STN → GPi → SNr → OFC
5	Th → Am → ACC → VTA → NAc → GPe → STN → SNr → GPi → OFC
6	Th → Am → ACC → VTA → NAc → GPe → STN → GPi → SNr → OFC
7	Th → Am → VTA → ACC → NAc → GPe → STN → SNr → GPi → OFC
8	Th → Am → VTA → ACC → NAc → GPe → STN → GPi → SNr → OFC
9	Th → VTA → Am → ACC → NAc → GPe → STN → SNr → GPi → OFC
10	Th → VTA → Am → ACC → NAc → GPe → STN → GPi → SNr → OFC
11	Th → VTA → ACC → Am → NAc → GPe → STN → SNr → GPi → OFC
12	Th → VTA → ACC → Am → NAc → GPe → STN → GPi → SNr → OFC

Table 8: Average Differences in Cycle Results After Reordering.

Option	Average Difference in Compulsions
1	0.000 ± 0.0000
2	0.126 ± 0.1613
3	0.114 ± 0.1491
4	0.128 ± 0.1654
5	0.132 ± 0.1792
6	0.140 ± 0.1765
7	0.111 ± 0.1497
8	0.130 ± 0.1640
9	0.136 ± 0.1837
10	0.109 ± 0.1447
11	0.132 ± 0.1681
12	0.135 ± 0.1808

N-Rays Test

The N-rays incident, in which a seemingly vital component was surreptitiously removed from physicist Prosper-René Blondlot's equipment during an experiment, resulting in no change in the results, is often used as a cautionary tale on the dangers of error due to experimenter bias [40]. Thus, the N-rays test for robustness is conducted by removing a significant part of the model and observing the resulting data. Assuming that the

removed portion is not extraneous, significant differences in the results should be observed. Table 9 shows the orders resulting from the elimination of each automaton.

Table 9: Possible Automata Eliminations.*

Option	Eliminated Automaton	Revised Order
1	Thalamus	ACC → Am → VTA → NAc → GPe → STN → SNr → GPi → OFC
2	ACC	Th → Am → VTA → NAc → GPe → STN → SNr → GPi → OFC
3	Amygdala	Th → ACC → VTA → NAc → GPe → STN → SNr → GPi → OFC
4	VTA	Th → ACC → Am → NAc → GPe → STN → SNr → GPi → OFC
5	Nucleus accumbens	Th → ACC → Am → VTA → SNr → GPi → OFC
6	GPe	Th → ACC → Am → VTA → NAc → STN → SNr → GPi → OFC
7	STN	Th → ACC → Am → VTA → NAc → GPe → SNr → GPi → OFC
8	Substantia nigra	Th → ACC → Am → VTA → NAc → GPe → STN → GPi → OFC
9	GPi	Th → ACC → Am → VTA → NAc → GPe → STN → SNr → OFC
10	OFC	Th → ACC → Am → VTA → NAc → GPe → STN → SNr → GPi

* Because the nucleus accumbens is the only entry into the indirect pathway, its elimination also results in the elimination of the GPe and STN.

Table 10: Average Differences in Cycle Results After Elimination.

Option	Eliminated Automaton	Average Difference in Compulsions
1	Thalamus	0.131 ± 0.1746
2	ACC	0.138 ± 0.1850
3	Amygdala	0.148 ± 0.2046
4	VTA	0.111 ± 0.1484
5	Nucleus accumbens	0.119 ± 0.1515
6	GPe	0.116 ± 0.1564
7	STN	0.136 ± 0.1715
8	Substantia nigra	0.129 ± 0.1751
9	GPi	0.124 ± 0.1573
10	OFC	0.152 ± 0.1985

CHAPTER FOUR:
CONCLUSIONS AND FUTURE WORK

Through the course of this thesis we have addressed issues with the current methods of diagnosing and treating obsessive-compulsive disorder. The main issues are with the use of magnetic resonance to map brain functions during symptom provocation. We have raised additional concerns in regard to the use of SSRI to treat OCD, given its differing pathologies as compared to depression.

An examination of a clinical study performed with OCD patients was also provided. We addressed the lack of statistical validity, as well as the implications for the heterogeneous nature of different obsessive-compulsive subtypes. However, we were also able to display a starting point for testing the accuracy for our model.

Through our model, we have shown that compulsive behavior can be roughly estimated by a function of previous compulsions performed and the severity of anxiety caused by external stimuli. Furthermore, our model suggests that compulsive behavior will increase as previous compulsions increase. This implies that compulsivity may be self-perpetuating.

Analysis

As stated previously, this work is to be considered preliminary and the results anecdotal. The model displays considerably less variance than observed in the test subjects. This may indicate a greater suitability for modeling aggregates of patients than generic individuals, but modifications of the model may improve its simulations of individual patients. Additionally, the results observed from our model appear to correlate more closely with contamination subtypes than with checking.

Future Work

The main phenomenon observed by our model was the increase in compulsive behavior with increasing previous compulsions. While this mirrors clinical observations, our model introduced an external counter to

maintain the value of previous compulsions. It is unlikely that the worry circuit has a dedicated counter with this function. Therefore, further research is warranted to eliminate the counter, while still accommodating the state reset, and discover what neural mechanisms actually create this phenomenon.

In addition, the model stops computing whenever a cycle ends without an additional compulsion. While this provides a clear means of recognizing a break in compulsive behavior, it does not account for individuals who may avoid compulsions for a short period of time, and then resume. In order to account for such delays, the model would have to integrate a mechanism for determining the duration of a "pause," as well as for lowering the sensitivity to previous compulsions over time.

Finally, as discussed throughout this thesis, OCD is largely heterogeneous. Our model has only been tested using experimental data for contamination and checking pathologies. Adjustments should be made in future to accommodate multiple subtypes.

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APPENDIX A:

IRB EXEMPTION LETTER

USF
UNIVERSITY OF
SOUTH FLORIDA

RESEARCH INTEGRITY AND COMPLIANCE
Institutional Review Boards, FWA No. 00001669
12901 Bruce B. Downs Blvd., MDC035 • Tampa, FL 33612-4799
(813) 974-5638 • FAX (813) 974-7091

9/28/2017

Lindsay Fields
Mathematics & Statistics
7345 Bonita Vista Way 101
Tampa, FL 33617

RE: **Not Human Subjects Research Determination**
IRB#: Pro00032306
Title: Developing a Predictive Model for Compulsive Behavior in Individuals with OCD

Dear Ms. Fields:

The Institutional Review Board (IRB) has reviewed your application. The activities presented in the application involve methods of program evaluation, quality improvement, and/or needs analysis. While potentially informative to others outside of the university community, study results would not appear to contribute to generalizable knowledge. As such, the activities do not meet the definition of human subject research under USF IRB policy, and USF IRB approval and oversight are therefore not required.

While not requiring USF IRB approval and oversight, your study activities should be conducted in a manner that is consistent with the ethical principles of your profession. If the scope of your project changes in the future, please contact the IRB for further guidance.

If you will be obtaining consent to conduct your study activities, please remove any references to "research" and do not include the assigned Protocol Number or USF IRB contact information.

If your study activities involve collection or use of health information, please note that there may be requirements under the HIPAA Privacy Rule that apply. For further information, please contact a HIPAA Program administrator at (813) 974-5638.

Sincerely,

Kristen Salomon, Ph.D., Vice Chairperson
USF Institutional Review Board

APPENDIX B:

DIAGNOSTIC SCALES

Beck Depression Inventory

The BDI-II was a 1996 revision of the BDI, which changed many of the diagnostic criteria for depression [2]. A general example is given below.

BECK DEPRESSION INVENTORY

This depression inventory can be self-scored. The scoring scale is at the end of the questionnaire.

1.
   - 0 I do not feel sad.
   - 1 I feel sad.
   - 2 I am sad all the time and I can't snap out of it.
   - 3 I am so sad and unhappy that I can't stand it.

2.
   - 0 I am not particularly discouraged about the future.
   - 1 I feel discouraged about the future.
   - 2 I feel I have nothing to look forward to.
   - 3 I feel the future is hopeless and that things cannot improve.

3.
   - 0 I do not feel like a failure.
   - 1 I feel I have failed more than the average person.
   - 2 As I look back on my life, all I can see is a lot of failures.
   - 3 I feel I am a complete failure as a person.

4.
   - 0 I get as much satisfaction out of things as I used to.
   - 1 I don't enjoy things the way I used to.
   - 2 I don't get real satsfaction out of anything anymore.
   - 3 I am dissatisfied or bored with everything.

5.
   - 0 I don't feel particularly guilty
   - 1 I feel guilty a good part of the time.
   - 2 I feel quite guilty most of the time.
   - 3 I feel guilty all of the time.

6.
   - 0 I don't feel I am being punished.
   - 1 I feel I may be punished.

2 I expect to be punished.
3 I feel I am being punished.

7.
0 I don't feel disappointed in myself.
1 I am disappointed in myself.
2 I am disgusted with myself.
3 I hate myself.

8.
0 I don't feel I am any worse than anybody else.
1 I am critical of myself for my weaknesses or mistakes.
2 I blame myself all the time for my faults.
3 I blame myself for everything bad that happens.

9.
0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10.
0 I don't cry any more than usual.
1 I cry more now than I used to.
2 I cry all the time now.
3 I used to be able to cry, but now I can't cry even though I want to.

11.
0 I am no more irritated by things than I ever was.
1 I am slightly more irritated now than usual.
2 I am quite annoyed or irritated a good deal of the time.
3 I feel irritated all the time.

12.
0 I have not lost interest in other people.
1 I am less interested in other people than I used to be.
2 I have lost most of my interest in other people.
3 I have lost all of my interest in other people.

13.
0 I make decisions about as well as I ever could.
1 I put off making decisions more than I used to.
2 I have greater difficulty in making decisions than I used to.
3 I can't make decisions at all anymore.

14.
0 I don't feel that I look any worse than I used to.
1 I am worried that I am looking old or unattractive.
2 I feel there are permanent changes in my appearance that make me look unattractive.
3 I believe that I look ugly.

15.
0 I can work about as well as before.
1 It takes an extra effort to get started at doing something.
2 I have to push myself very hard to do anything.
3 I can't do any work at all.

16.
- 0 I can sleep as well as usual.
- 1 I don't sleep as well as I used to.
- 2 I wake up 1-2 hours earlier than usual and find it hard to go back to sleep.
- 3 I wake up several hours earlier than I used to and cannot get back to sleep.

17.
- 0 I don't get more tired than usual.
- 1 I get tired more easily than I used to.
- 2 I get tired from doing almost anything.
- 3 I am too tired to do anything.

18.
- 0 My appetite is no worse than usual.
- 1 My appetite is not as good as it used to be.
- 2 My appetite is much worse now.
- 3 I have no appetite at all anymore.

19.
- 0 I haven't lost much weight, if any, lately.
- 1 I have lost more than five pounds.
- 2 I have lost more than ten pounds.
- 3 I have lost more than fifteen pounds.

20.
- 0 I am no more worried about my health than usual.
- 1 I am worried about physical problems like aches, pains, upset stomach, or constipation.
- 2 I am very worried about physical problems and it's hard to think of much else.
- 3 I am so worried about my physical problems that I cannot think of anything else.

21.
- 0 I have not noticed any recent change in my interest in sex.
- 1 I am less interested in sex than I used to be.
- 2 I have almost no interest in sex.
- 3 I have lost interest in sex completely.

INTERPRETING THE BECK DEPRESSION INVENTORY

Now that you have completed the questionnaire, add up the score for each of the twenty-one questions by counting the number to the right of each question you marked. The highest possible total for the whole test would be sixty-three. This would mean you circled number three on all twenty-one questions. Since the lowest possible score for each question is zero, the lowest possible score for the test would be zero. This would mean you circles zero on each question. You can evaluate your depression according to the table below.

Total Score _____
Levels of Depression:
1-10 = These ups and downs are considered normal
11-16 = Mild mood disturbance
17-20 = Borderline clinical depression
21-30 = Moderate depression
31-40 = Severe depression
over 40 = Extreme depression

Clinical Global Impressions Scale

The CGI consists of two measures evaluating: (1) the severity of mental illness on a scale from 1 to 7 and (2) the change in mental health from the initiation of treatment. There are no universally accepted scoring guidelines for the seven diagnostic points of the CGI; rather they were designed to be based upon the clinical judgment of the diagnosing physician. Tables 11 and 12 display generic guidelines for mental illness severity and mental health improvement used in clinical research [5].

Table 11: Clinical Global Impressions Severity Scale (CGI-S).

Score	Impression	Description
1	Normal	Not at all ill, symptoms of disorder not present past seven days
2	Borderline mentally ill	Subtle or suspected pathology
3	Mildly ill	Established symptoms with minimal distress or difficulty in social and occupational function
4	Moderately ill	Overt symptoms causing noticeable functional impairment or distress
5	Markedly ill	Intrusive symptoms that distinctly impair social/occupational function or cause intrusive levels of distress
6	Severely ill	Disruptive pathology, behavior and function are influenced by symptoms
7	Extremely ill	Pathology drastically interferes in many life functions; may be hospitalized

Table 12: Clinical Global Impressions Improvement Scale (CGI-I).

Score	Impression	Description
1	Very much improved	Good level of functioning; minimal symptoms; represents a substantial change
2	Much improved	Notably better with significant reduction of symptoms
3	Minimally improved	Slightly better; little or no clinically meaningful reduction of symptoms
4	No change	Symptoms remain essentially unchanged
5	Minimally worse	Slightly worse but may not be clinically meaningful
6	Much worse	Clinically significant increase in symptoms and diminished functioning
7	Very much worse	Severe exacerbation of symptoms and loss of functioning

Yale-Brown Obsessive Compulsive Scale

This scale is designed to rate the severity and type of symptoms in patients with OCD. In general, the items depend on the patient's report; however, the final rating is based on the physician's clinical judgment. The final score for each item reflects a composite rating of all of the patient's obsessions or compulsions.

All 19 items are rated, but only items 1-10 (excluding items 1b and 6b) are used to determine the total Y-BOCS score. The total score is the sum of items 1-10 (excluding 1b and 6b), whereas the obsession subtotal is the sum of items 1-5 (excluding lb) and the compulsive subtotal is the sum of items 6-10 (excluding 6b) [13].

1. TIME OCCUPIED BY OBSESSIVE THOUGHTS
   Q: How much of your time is occupied by obsessive thoughts? [When obsessions occur as brief, intermittent intrusions, it may be difficult to assess time occupied by them in terms of total hours. In such cases, estimate time by determining how frequently they occur. Consider both the number of times the intrusions occur and how many hours of the day are affected.
   0 = None.
   1 = Mild, less than 1 hr/day or occasional intrusion.
   2 = Moderate, 1 to 3 hrs/day or frequent intrusion.
   3 = Severe, greater than 3 and up to 8 hrs/day or very frequent intrusion.
   4 = Extreme, greater than 8 hrs/day or near constant intrusion.

1b. OBSESSION-FREE INTERVAL (not included in total score)
   Q: On the average, what is the longest number of consecutive waking hours per day that you are completely free of obsessive thoughts?
   0 = No symptoms.
   1 = Long symptom-free interval, more than 8 consecutive hours/day symptom-free.
   2 = Moderately long symptom-free interval, more than 3 and up to 8 consecutive hours/day symptom-free.
   3 = Short symptom-free interval, from 1 to 3 consecutive hours/day symptom-free.
   4 = Extremely short symptom-free interval, less than 1 consecutive hour/day symptom-free.

2. INTERFERENCE DUE TO OBSESSIVE THOUGHTS
   Q: How much do your obsessive thoughts interfere with your social or work (or role) functioning? Is there anything that you don't do because of them?
   0 = None.
   1 = Mild, slight interference with social or occupational activities, but overall performance not impaired.
   2 = Moderate, definite interference with social or occupational performance, but still manageable.
   3 = Severe, causes substantial impairment in social or occupational performance.
   4 = Extreme, incapacitating.

3. DISTRESS ASSOCIATED WITH OBSESSIVE THOUGHTS
   Q: How much distress do your obsessive thoughts cause you?
   0 = None.
   1 = Mild, not too disturbing.

2 = Moderate, disturbing, but still manageable.
3 = Severe, very disturbing.
4 = Extreme, near constant and disabling distress.

4. RESISTANCE AGAINST OBSESSIONS

Q: How much of an effort do you make to resist the obsessive thoughts? How often do you try to disregard or turn your attention away from these thoughts as they enter your mind? [Only rate effort made to resist, not success or failure in actually controlling the obsessions.]

0 = Makes an effort to always resist, or symptoms so minimal doesn't need to actively resist.
1 = Tries to resist most of the time.
2 = Makes some effort to resist.
3 = Yields to all obsessions without attempting to control them, but does so with some reluctance.
4 = Completely and willingly yields to all obsessions.

5. DEGREE OF CONTROL OVER OBSESSIVE THOUGHTS

Q: How much control do you have over your obsessive thoughts? How successful are you in stopping or diverting your obsessive thinking? Can you dismiss them?

0 = Complete control.
1 = Much control, usually able to stop or divert obsessions with some effort and concentration.
2 = Moderate control, sometimes able to stop or divert obsessions.
3 = Little control, rarely successful in stopping or dismissing obsessions, can only divert attention with difficulty.
4 = No control, experienced as completely involuntary, rarely able to even momentarily alter obsessive thinking.

6. TIME SPENT PERFORMING COMPULSIVE BEHAVIORS

Q: How much time do you spend performing compulsive behaviors? [When compulsions occur as brief, intermittent behaviors, it may difficult to assess time spent performing them in terms of total hours. In such cases, estimate time by determining how frequently they are performed. Consider both the number of times compulsions are performed and how many hours of the day are affected. Count separate occurrences of compulsive behaviors, not number of repetitions.]

0 = None.
1 = Mild (spends less than 1 hr/day performing compulsions), or occasional performance of compulsive behaviors.
2 = Moderate (spends from 1 to 3 hrs/day performing compulsions), or frequent performance of compulsive behaviors.
3 = Severe (spends more than 3 and up to 8 hrs/day performing compulsions), or very frequent performance of compulsive behaviors.
4 = Extreme (spends more than 8 hrs/day performing compulsions), or near constant performance of compulsive behaviors (too numerous to count).

6b. COMPULSION-FREE INTERVAL (not included in total score)

Q: On the average, what is the longest number of consecutive waking hours per day that you are completely free of compulsive behavior?

0 = No symptoms.
1 = Long symptom-free interval, more than 8 consecutive hours/day symptom-free.
2 = Moderately long symptom-free interval, more than 3 and up to 8 consecutive hours/day symptom-free.

3 = Short symptom-free interval, from 1 to 3 consecutive hours/day symptom-free.
4 = Extremely short symptom-free interval, less than 1 consecutive hour/day symptom-free.

7. INTERFERENCE DUE TO COMPULSIVE BEHAVIORS

Q: How much do your compulsive behaviors interfere with your social or work (or role) functioning? Is there anything that you don't do because of the compulsions?

0 = None.
1 = Mild, slight interference with social or occupational activities, but overall performance not impaired.
2 = Moderate, definite interference with social or occupational performance, but still manageable.
3 = Severe, causes substantial impairment in social or occupational performance.
4 = Extreme, incapacitating.

8. DISTRESS ASSOCIATED WITH COMPULSIVE BEHAVIOR

Q: How would you feel if prevented from performing your compulsions? How anxious would you become?

0 = None.
1 = Mild only slightly anxious if compulsions prevented, or only slight anxiety during performance of compulsions.
2 = Moderate, reports that anxiety would mount but remain manageable if compulsions prevented, or that anxiety increases but remains manageable during performance of compulsions.
3 = Severe, prominent and very disturbing increase in anxiety if compulsions interrupted, or prominent and very disturbing increase in anxiety during performance of compulsions.
4 = Extreme, incapacitating anxiety from any intervention aimed at modifying activity, or incapacitating anxiety develops during performance of compulsions.

9. RESISTANCE AGAINST COMPULSIONS

Q: How much of an effort do you make to resist the compulsions? [Only rate effort made to resist, not success or failure in actually controlling the compulsions.]

0 = Makes an effort to always resist, or symptoms so minimal doesn't need to actively resist.
1 = Tries to resist most of the time.
2 = Makes some effort to resist.
3 = Yields to almost all compulsions without attempting to control them, but does so with some reluctance.
4 = Completely and willingly yields to all compulsions.

10. DEGREE OF CONTROL OVER COMPULSIVE BEHAVIOR

Q: How strong is the drive to perform the compulsive behavior? How much control do you have over the compulsions?

0 = Complete control.
1 = Much control, experiences pressure to perform the behavior but usually able to exercise voluntary control over it.
2 = Moderate control, strong pressure to perform behavior, can control it only with difficulty.
3 = Little control, very strong drive to perform behavior, must be carried to completion, can only delay with difficulty.
4 = No control, drive to perform behavior experienced as completely involuntary and overpowering, rarely able to even momentarily delay activity.

11. INSIGHT INTO OBSESSIONS AND COMPULSIONS

Q: Do you think your concerns or behaviors are reasonable? What do you think would happen if you did not perform the compulsion(s)? Are you convinced something would really happen?

0 = Excellent insight, fully rational.

1 = Good insight. Readily acknowledges absurdity or excessiveness of thoughts or behaviors but does not seem completely convinced that there isn't something besides anxiety to be concerned about.

2 = Fair insight. Reluctantly admits thoughts or behavior seem unreasonable or excessive, but wavers. May have some unrealistic fears, but no fixed convictions.

3 = Poor insight. Maintains that thoughts or behaviors are not unreasonable or excessive, but acknowledges validity of contrary evidence (i.e., overvalued ideas present).

4 = Lacks insight, delusional. Definitely convinced that concerns and behavior are reasonable, unresponsive to contrary evidence.

12. AVOIDANCE

Q: Have you been avoiding doing anything, going any place, or being with anyone because of your obsessional thoughts or out of concern you will perform compulsions?

0 = No deliberate avoidance.

1 = Mild, minimal avoidance.

2 = Moderate, some avoidance; clearly present.

3 = Severe, much avoidance; avoidance prominent.

4 = Extreme, very extensive avoidance; patient does almost everything he/she can to avoid triggering symptoms.

13. DEGREE OF INDECISIVENESS

Q: Do you have trouble making decisions about little things that other people might not think twice about (e.g., which clothes to put on in the morning; which brand of cereal to buy)?

0 = None.

1 = Mild, some trouble making decisions about minor things.

2 = Moderate, freely reports significant trouble making decisions that others would not think twice about.

3 = Severe, continual weighing of pros and cons about nonessentials.

4 = Extreme, unable to make any decisions. Disabling.

14. OVERVALUED SENSE OF RESPONSIBILITY

Q: Do you feel very responsible for the consequences of your actions? Do you blame yourself for the outcome of events not completely in your control?

0 = None.

1 = Mild, only mentioned on questioning, slight sense of over-responsibility.

2 = Moderate, ideas stated spontaneously, clearly present; patient experiences significant sense of over-responsibility for events outside his/her reasonable control.

3 = Severe, ideas prominent and pervasive; deeply concerned he/she is responsible for events clearly outside his control. Self-blaming far-fetched and nearly irrational.

4 = Extreme, delusional sense of responsibility.

15. PERVASIVE SLOWNESS/ DISTURBANCE OF INERTIA

Q: Do you have difficulty starting or finishing tasks? Do many routine activities take longer than they should?

0 = None.
1 = Mild, occasional delay in starting or finishing.
2 = Moderate, frequent prolongation of routine activities but tasks usually completed. Frequently late.
3 = Severe, pervasive and marked difficulty initiating and completing routine tasks. Usually late.
4 = Extreme, unable to start or complete routine tasks without full assistance.

16. PATHOLOGICAL

Q: After you complete an activity do you doubt whether you performed it correctly? Do you doubt whether you did it at all? When carrying out routine activities do you find that you don't trust your senses?

0 = None.
1 = Mild, only mentioned on questioning, slight pathological doubt. Examples given may be within normal range.
2 = Moderate, ideas stated spontaneously, clearly present and apparent in some of patient's behaviors; patient bothered by significant pathological doubt. Some effect on performance but still manageable.
3 = Severe, uncertainty about perceptions or memory prominent; pathological doubt frequently affects performance.
4 = Extreme, uncertainty about perceptions constantly present; pathological doubt substantially affects almost all activities.

17. GLOBAL SEVERITY: Interviewer's judgement of the overall severity of the patient's illness. Rated from 0 (no illness) to 6 (most severe patient seen)

0 = No illness.
1 = Illness slight, doubtful, transient; no functional impairment.
2 = Mild symptoms, little functional impairment.
3 = Moderate symptoms, functions with effort.
4 = Moderate - Severe symptoms, limited functioning.
5 = Severe symptoms, functions mainly with assistance.
6 = Extremely Severe symptoms, completely nonfunctional.

18. GLOBAL IMPROVEMENT

0 = Very much worse.
1 = Much worse.
2 = Minimally worse.
3 = No change.
4 = Minimally improved.
5 = Much improved.
6 = Very much improved.

19. RELIABILITY

0 = Excellent, no reason to suspect data unreliable.
1 = Good, factor(s) present that may adversely affect reliability.
2 = Fair, factor(s) present that definitely reduce reliability.
3 = Poor, very low reliability.

APPENDIX C:
ADDITIONAL TABLES

Table 13: Simulated Characteristics at Varying Previous Compulsions.

Trigger Severity	Previous Compulsions	Final Compulsions
1	0	1.840 ± 2.3942
	1	2.787 ± 2.3076
	2	3.991 ± 2.4105
	3	4.846 ± 2.2586
	4	5.857 ± 2.3520
	5	6.916 ± 2.4234
	6	7.992 ± 2.5362
	7	8.812 ± 2.2144
	8	9.921 ± 2.1885
	9	11.090 ± 2.5044
	10	11.889 ± 2.3397
2	0	1.926 ± 2.4051
	1	2.984 ± 2.5168
	2	3.985 ± 2.3888
	3	4.820 ± 2.2425
	4	6.100 ± 2.6921
	5	6.809 ± 2.2471
	6	8.005 ± 2.4143
	7	9.126 ± 2.5657
	8	10.028 ± 2.5651
	9	11.113 ± 2.5339
	10	12.047 ± 2.4287
3	0	2.130 ± 2.5553
	1	3.013 ± 2.5356
	2	4.224 ± 2.7224
	3	5.261 ± 2.6563
	4	6.195 ± 2.5767
	5	7.101 ± 2.4962
	6	8.191 ± 2.7872
	7	9.305 ± 2.8653
	8	10.310 ± 2.6334
	9	11.321 ± 2.7828
	10	12.266 ± 2.6598

Table 13 (Continued)

Trigger Severity	Previous Compulsions	Final Compulsions
4	0	2.278 ± 2.8104
	1	3.285 ± 2.8488
	2	4.326 ± 2.7293
	3	5.207 ± 2.7014
	4	6.235 ± 2.6572
	5	7.380 ± 2.9736
	6	8.381 ± 3.1054
	7	9.440 ± 2.9143
	8	10.413 ± 2.9697
	9	11.330 ± 2.8441
	10	12.589 ± 3.0954
5	0	2.452 ± 2.8245
	1	3.454 ± 3.1083
	2	4.477 ± 2.8934
	3	5.483 ± 2.9337
	4	6.625 ± 3.1139
	5	7.442 ± 2.8581
	6	8.501 ± 2.9138
	7	9.558 ± 3.0430
	8	10.672 ± 3.2807
	9	11.748 ± 3.1753
	10	12.827 ± 3.3024
6	0	2.701 ± 3.3125
	1	3.594 ± 3.0791
	2	4.794 ± 3.2178
	3	5.633 ± 3.0554
	4	6.662 ± 3.1365
	5	7.985 ± 3.4642
	6	8.848 ± 3.4130
	7	9.958 ± 3.5029
	8	10.950 ± 3.5336
	9	11.878 ± 3.2597
	10	12.771 ± 3.4953
7	0	3.052 ± 3.7028
	1	4.017 ± 3.5746
	2	4.801 ± 3.4224
	3	6.187 ± 3.8271
	4	6.739 ± 3.4425
	5	8.162 ± 3.6167
	6	8.911 ± 3.4443
	7	10.065 ± 3.5428
	8	11.244 ± 3.7455
	9	12.298 ± 3.8026
	10	13.197 ± 3.7739

Table 13 (Continued)

Trigger Severity	Previous Compulsions	Final Compulsions
8	0	3.122 ± 3.7007
	1	4.158 ± 3.9700
	2	5.395 ± 3.8820
	3	6.498 ± 4.2774
	4	7.390 ± 4.3242
	5	8.456 ± 4.0123
	6	9.398 ± 4.0608
	7	10.311 ± 4.1033
	8	11.653 ± 4.7086
	9	12.508 ± 4.0702
	10	13.592 ± 3.9967
9	0	3.689 ± 4.2585
	1	4.709 ± 7.6038
	2	5.909 ± 4.5707
	3	6.733 ± 4.6255
	4	8.037 ± 4.9912
	5	8.792 ± 4.5567
	6	9.771 ± 4.2236
	7	11.155 ± 5.3426
	8	11.787 ± 4.4251
	9	13.269 ± 5.2148
	10	14.257 ± 5.3018
10	0	4.051 ± 4.7342
	1	5.350 ± 5.1974
	2	6.572 ± 5.4467
	3	7.287 ± 5.0916
	4	8.441 ± 5.4013
	5	9.354 ± 5.2494
	6	10.631 ± 5.2728
	7	11.675 ± 5.9188
	8	13.253 ± 8.4564
	9	13.872 ± 5.9699
	10	14.897 ± 5.7765

APPENDIX D:

SOURCE CODE

The Run.m file is the main compiler which calls several functions, each representing a separate automaton, and then plots the final number of compulsions. The file runs for 1000 iterations to properly estimate the results.

```
cd(tempdir); % Open directory

fileID = fopen('Table.txt', 'w+'); % Clear table
fclose(fileID);

compulsions = 0; % Define number of compulsions

max_compulsions = 10; % Define maximum number of compulsions

trigger = input('Trigger severity?\n'); % Input trigger severity

while compulsions <= max_compulsions
        iterations = 1; % Define number of iterations

        max_iterations = 1000; % Define maximum number of iterations

        while iterations <= max_iterations
                prior = compulsions;

                % Thalamus inputs
                ACCTh = 1; % Normal = 0; excited = 1
                AmTh = 1; % Normal = 0; excited = 1
                VTATh = 1; % Normal = 0; excited = 1; inhibited = -1
                NAcTh = 1; % Normal = 0; excited = 1
                OFCTh = 1; % Normal = 0; excited = 1

                % ACC inputs
                ACCACC = 0; % Normal = 0; inhibited = -1
                AmACC = 1; % Normal = 0; excited = 1
                VTAACC = 1; % Normal = 0; excited = 1; inhibited = -1
                OFCACC = 1; % Normal = 0; excited = 1
```

```
% Amygdala inputs
AmAm = 0; % Normal = 0; inhibited = -1
VTAAm = 1; % Normal = 0; excited = 1; inhibited = -1
OFCAm = 0; % Normal = 0; inhibited = -1

% VTA inputs
VTAVTA = 0; % Normal = 0; inhibited = -1
NAcVTA = 1; % Normal = 0; excited = 1
OFCVTA = 1; % Normal = 0; excited = 1

% NAc inputs
AmNAc = 2; % Normal = 0; excited = 1; highly excited = 2
OFCNAc = 2; % Normal = 0; excited = 1; highly excited = 2

% STN inputs
GPeSTN = 0; % Normal = 0; inhibited = -1

% SNr inputs
STNSNr = 1; % Normal = 0; excited = 1
GPiSNr = 1; % Normal = 0; excited = 1; inhibited = -1

% GPi inputs
STNGPi = 1; % Normal = 0; excited = 1

% OFC inputs
OFCOFC = 0; % Normal = 0; inhibited = -1

% Each automaton is called individually
[ThACC, ThAm, ThVTA, ThOFC] = Th(ACCTh, AmTh, VTATh, NAcTh, OFCTh, compulsions, trigger); % Call thalamus
[ACCTh, ACCACC, ACCAm, ACCVTA] = ACC(ThACC, ACCACC, AmACC, VTAACC, OFCACC, compulsions, trigger); % Call ACC
[AmTh, AmACC, AmAm, AmVTA, AmNAc, AmOFC] = Am(ThAm, ACCAm, AmAm, VTAAm, OFCAm, AmNAc, OFCNAc, compulsions, trigger); % Call amygdala
[VTATh, VTAACC, VTAAm, VTAVTA, VTANAc, VTAOFC] = VTA(ThVTA, ACCVTA, AmVTA, VTAVTA, NAcVTA, OFCVTA, compulsions, trigger); % Call VTA
[NAcTh, NAcVTA, NAcGPe, NAcSNr, NAcGPi] = NAc(AmNAc, VTANAc, OFCNAc, compulsions, trigger); % Call nucleus accumbens
if NAcGPe == 1 % Indirect pathway
    [GPeSTN] = GPe(NAcGPe, compulsions, trigger); % Call GPe
    [STNSNr, STNGPi] = STN(GPeSTN, compulsions, trigger); % Call STN
end
[SNrOFC, SNrGPi] = SNr(NAcSNr, STNSNr, GPiSNr, compulsions, trigger); % Call substantia nigra
[GPiOFC, GPiSNr] = GPi(NAcGPi, STNGPi, SNrGPi, compulsions, trigger); % Call GPi
[OFCTh, OFCACC, OFCAm, OFCVTA, OFCNAc, OFCOFC, probability] = OFC(ThOFC, AmOFC, VTAOFC, SNrOFC, GPiOFC, OFCOFC, compulsions, trigger); % Call OFC
```

```
% When probability reaches 0.375, a compulsion is performed and the cycle restarts
while probability >= 0.375 && compulsions <= 200 % 200 compulsions is infinite
    compulsions = compulsions + 1; % Increase compulsions

    % All inputs are reset to normal
    ACCTh = 0;
    AmTh = 0;
    VTATh = 0;
    NAcTh = 0;
    OFCTh = 0;

    ACCACC = 0;
    AmACC = 0;
    VTAACC = 0;
    OFCACC = 0;

    AmAm = 0;
    VTAAm = 0;
    OFCAm = 0;

    VTAVTA = 0;
    NAcVTA = 0;
    OFCVTA = 0;

    AmNAc = 0;
    OFCNAc = 0;

    GPeSTN = 0;

    STNSNr = 0;
    GPiSNr = 0;

    STNGPi = 0;

    OFCOFC = 0;

    % Each automaton is called again
    [ThACC, ThAm, ThVTA, ThOFC] = Th(ACCTh, AmTh, VTATh, NAcTh, OFCTh,
compulsions, trigger);
    [ACCTh, ACCACC, ACCAm, ACCVTA] = ACC(ThACC, ACCACC, AmACC,
VTAACC, OFCACC, compulsions, trigger);
    [AmTh, AmACC, AmAm, AmVTA, AmNAc, AmOFC] = Am(ThAm, ACCAm,
AmAm, VTAAm, OFCAm, AmNAc, OFCNAc, compulsions, trigger);
    [VTATh, VTAACC, VTAAm, VTAVTA, VTANAc, VTAOFC] = VTA(ThVTA,
ACCVTA, AmVTA, VTAVTA, NAcVTA, OFCVTA, compulsions, trigger);
    [NAcTh, NAcVTA, NAcGPe, NAcSNr, NAcGPi] = NAc(AmNAc, VTANAc,
OFCNAc, compulsions, trigger);
    if NAcGPe == 1
```

```
                    [GPeSTN] = GPe(NAcGPe, compulsions, trigger);
                    [STNSNr, STNGPi] = STN(GPeSTN, compulsions, trigger);
                end
                [SNrOFC, SNrGPi] = SNr(NAcSNr, STNSNr, GPiSNr, compulsions, trigger);
                [GPiOFC, GPiSNr] = GPi(NAcGPi, STNGPi, SNrGPi, compulsions, trigger);
                [OFCTh, OFCACC, OFCAm, OFCVTA, OFCNAc, OFCOFC, probability] =
OFC(ThOFC, AmOFC, VTAOFC, SNrOFC, GPiOFC, OFCOFC, compulsions, trigger);
            end

            % Input number of compulsions to table
            fileID = fopen('Table.txt', 'a+');
            fprintf(fileID,'%6i %6i\r\n',prior,compulsions);
            fclose(fileID);

            iterations = iterations + 1; % Increase iterations
            compulsions = prior; % Reset compulsions
        end
        compulsions = compulsions + 1; % Increase compulsions
end

% Collect results
load Table.txt
s0 = Table(1:max_iterations,2);
s1 = Table((max_iterations+1):(2*max_iterations),2);
s2 = Table((2*max_iterations+1):(3*max_iterations),2);
s3 = Table((3*max_iterations+1):(4*max_iterations),2);
s4 = Table((4*max_iterations+1):(5*max_iterations),2);
s5 = Table((5*max_iterations+1):(6*max_iterations),2);
s6 = Table((6*max_iterations+1):(7*max_iterations),2);
s7 = Table((7*max_iterations+1):(8*max_iterations),2);
s8 = Table((8*max_iterations+1):(9*max_iterations),2);
s9 = Table((9*max_iterations+1):(10*max_iterations),2);
s10 = Table((10*max_iterations+1):(11*max_iterations),2);

matrix = [s0, s1, s2, s3, s4, s5, s6, s7, s8, s9, s10];
mean = mean(matrix)
deviation = std(matrix)
```

```
% Thalamus Behavior
function [ThACC, ThAm, ThVTA, ThOFC] = Th(ACCTh, AmTh, VTATh, NAcTh, OFCTh, compulsions,
trigger)

bound = (0.002 * compulsions) + (0.02 * trigger); % Define lower bound

if ACCTh == 1 % ACC excites the thalamus
        bound = bound + 0.005;
end

if AmTh == 1 % Amygdala excites the thalamus
        bound = bound + 0.01;
end

if VTATh == 1 % VTA excites the thalamus
        bound = bound + 0.005;
elseif VTATh == -1 % VTA inhibits the thalamus
        bound = bound - 0.01;
end

if NAcTh == 1 % Nucleus accumbens excites the thalamus
        bound = bound + 0.005;
end

if OFCTh == 1 % OFC excites the thalamus
        bound = bound + 0.01;
end

probability = bound + (1 - bound).*rand; % Selects a random value between the lower bound and 1

if probability >= 0.525 % Thalamus is excited
        ThACC = 1; % Thalamus excites the ACC
        ThAm = 1; % Thalamus excites the amygdala
        ThVTA = 1; % Thalamus excites the VTA
        ThOFC = 1; % Thalamus excites the OFC
else % Thalamus is unexcited
        ThACC = 0;
        ThAm = 0;
        ThVTA = 0;
        ThOFC = 0;
end
```

```
% Anterior Cingulate Cortex Behavior
function [ACCTh, ACCACC, ACCAm, ACCVTA] = ACC(ThACC, ACCACC, AmACC, VTAACC, OFCACC,
compulsions, trigger)

bound = (0.002 * compulsions) + (0.02 * trigger);

if ThACC == 1 % Thalamus excites the ACC
        bound = bound + 0.01;
end

if ACCACC == -1 % ACC inhibits itself
        bound = bound - 0.01;
end

if AmACC == 1 % Amygdala excites the ACC
        bound = bound + 0.01;
end

if VTAACC == 1 % VTA excites the ACC
        bound = bound + 0.005;
elseif VTAACC == -1 % VTA inhibits the ACC
        bound = bound - 0.01;
end

if OFCACC == 1 % OFC excites the ACC
        bound = bound + 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.525 % ACC is excited
        ACCTh = 1; % ACC excites the thalamus
        ACCACC = 0;
        ACCAm = 0;
        ACCVTA = 1; % ACC excites the VTA
else % ACC is unexcited
        ACCTh = 0;
        ACCACC = -1; % ACC inhibits itself
        ACCAm = -1; % ACC inhibits the amygdala
        ACCVTA = 0;
end
```

```
% Amygdala Behavior
function [AmTh, AmACC, AmAm, AmVTA, AmNAc, AmOFC] = Am(ThAm, ACCAm, AmAm, VTAAm,
OFCAm, AmNAc, OFCNAc, compulsions, trigger)

bound = (0.002 * compulsions) + (0.02 * trigger);

if ThAm == 1 % Thalamus excites the amygdala
        bound = bound + 0.01;
end

if ACCAm == -1 % ACC inhibits the amygdala
        bound = bound - 0.01;
end

if VTAAm == 1 % VTA excites the amygdala
        bound = bound + 0.005;
elseif VTAAm == -1 % VTA inhibits the amygdala
        bound = bound - 0.01;
end

if OFCAm == -1 % OFC inhibits the amygdala
        bound = bound - 0.02;
end

% When the OFC has excites the nucleus accumbens and the amygala excites or highly excites the nucleus
accumbens, self-inhibition inhibits the amygala
if OFCNAc == 1 && AmNAc >= 1 && AmAm == -1
        bound = bound - 0.02;
end

% When the OFC highly excites the nucleus accumbens and the amygala excites or highly excites the nucleus
accumbens, self-inhibition inhibits the amygala
if OFCNAc == 2 && AmNAc >= 1 && AmAm == -1
        bound = bound - 0.02;
end

% When the OFC highly excites the nucleus accumbens and the amygala has no impact on the nucleus
accumbens, self-inhibition excites the amygala
if OFCNAc == 2 && AmNAc == 0 && AmAm == -1
        bound = bound + 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.75 % Amygdala is highly excited
        AmTh = 1;
        AmACC = 1;
        AmAm = 0;
```

```
        AmVTA = 1;
        AmNAc = 2; % Amygdala highly excites the nucleus accumbens
        AmOFC = 1;
elseif probability >= 0.375 % Amygdala is excited
        AmTh = 1; % Amygdala excites the thalamus
        AmACC = 1; % Amygdala excites the ACC
        AmAm = 0;
        AmVTA = 1; % Amygdala excites the VTA
        AmNAc = 1; % Amygdala excites the nucleus accumbens
        AmOFC = 1; % Amygdala excites the OFC
else % Amygdala is unexcited
        AmTh = 0;
        AmACC = 0;
        AmAm = -1; % Amygdala inhibits itself
        AmVTA = 0;
        AmNAc = 0;
        AmOFC = 0;
end
```

```
% Ventral Tegmental Area Behavior
function [VTAThVTA, VTAACCVTA, VTAAmVTA, VTAVTAVTA, VTANAcVTA, VTAOFCVTA] = VTA(ThVTA, ACCVTA, AmVTA,
VTAVTA, NAcVTA, OFCVTA, compulsions, trigger)

bound = (0.002 * compulsions) + (0.02 * trigger);

if ThVTA == 1 % Thalamus excites the VTA
        bound = bound + 0.01;
end

if ACCVTA == 1 % ACC excites the VTA
        bound = bound + 0.005;
end

if AmVTA == 1 % Amygdala excites the VTA
        bound = bound + 0.01;
end

if VTAVTA == -1 % VTA inhibits itself
        bound = bound - 0.01;
end

if NAcVTA == 1 % Nucleus accumbens excites the VTA
        bound = bound + 0.005;
end

if OFCVTA == 1 % OFC excites the VTA
        bound = bound + 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.6 % VTA is excited
        VTAThVTA = 1; % VTA excites the thalamus
        VTAACCVTA = 1; % VTA excites the ACC
        VTAAmVTA = 1; % VTA excites the amygdala
        VTAVTAVTA = 0;
        VTANAcVTA = 1; % VTA excites the nucleus accumbens
        VTAOFCVTA = 1; % VTA excites the OFC
else % VTA is unexcited
        VTAThVTA = 0;
        VTAACCVTA = 0;
        VTAAmVTA = 0;
        VTAVTAVTA = -1; % VTA inhibits itself
        VTANAcVTA = -1; % VTA inhibits the nucleus accumbens
        VTAOFCVTA = 0;
end
```

```
% Nucleus Accumbens Behavior
function [NAcTh, NAcVTA, NAcGPe, NAcSNr, NAcGPi] = NAc(AmNAc, VTANAc, OFCNAc, compulsions, trigger)

bound = (0.002 * compulsions) + (0.02 * trigger);

if AmNAc == 2 % Amygdala highly excites the nucleus accumbens
        bound = bound + 0.02;
elseif AmNAc == 1 % Amygdala excites the nucleus accumbens
        bound = bound + 0.01;
end

if VTANAc == -1 % VTA inhibits the nucleus accumbens
        bound = bound - 0.005;
end

if OFCNAc == 2 % OFC highly excites the nucleus accumbens
        bound = bound + 0.02;
elseif OFCNAc == 1 % OFC excites the nucleus accumbens
        bound = bound + 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.9 % Nucleus accumbens is excited
        NAcTh = 1; % Nucleus accumbens excites the thalamus
        NAcVTA = 1; % Nucleus accumbens excites the VTA
        NAcGPe = 0;
        NAcSNr = 1; % Direct pathway
        NAcGPi = 1; % Direct pathway
else % Nucleus accumbens is unexcited
        NAcTh = 0;
        NAcVTA = 0;
        NAcGPe = 1; % Indirect pathway
        NAcSNr = 0;
        NAcGPi = 0;
end
```

```
% Global Pallidus Externa Behavior
function [GPeSTN] = GPe(NAcGPe, compulsions, trigger)

bound = (0.001 * compulsions) + (0.01 * trigger);

if NAcGPe == -1 % Indirect pathway
        bound = bound - 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.15 % GPe is excited
        GPeSTN = 0;
else % GPe is unexcited
        GPeSTN = -1; % GPe inhibits the STN
end
```

```
% Subthalamic Nucleus Behavior
function [STNSNr, STNGPi] = STN(GPeSTN, compulsions, trigger)

bound = (0.001 * compulsions) + (0.01 * trigger);

if GPeSTN == -1 % GPe inhibits STN
        bound = bound - 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.15 % STN is excited
        STNSNr = 1; % STN excites the substantia nigra
        STNGPi = 1; % STN excites the GPi
else % STN is unexcited
        STNSNr = 0;
        STNGPi = 0;
end
```

```
% Substantia Nigra Behavior
function [SNrGPi, SNrOFC] = SNr(NAcSNr, STNSNr, GPiSNr, compulsions, trigger)

bound = (0.002 * compulsions) + (0.02 * trigger);

if NAcSNr == 1 % Direct pathway
        bound = bound + 0;
end

if STNSNr == 1 % Indirect pathway
        bound = bound + 0.01;
end

if GPiSNr == -1 % GPi inhibits substantia nigra
        bound = bound - 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.15 % Substantia nigra is excited
        SNrGPi = 0;
        SNrOFC = 0;
else % Substantia nigra is unexcited
        SNrGPi = -1; % Substantia nigra inhibits the GPi
        SNrOFC = -1; % Substantia nigra inhibits the OFC
end
```

```
% Globus Pallidus Interna Behavior
function [GPiSNr, GPiOFC] = GPi(NAcGPi, STNGPi, SNrGPi, compulsions, trigger)

bound = (0.002 * compulsions) + (0.02 * trigger);

if NAcGPi == 1 % Direct pathway
        bound = bound + 0;
end

if STNGPi == 1 % Indirect pathway
        bound = bound + 0.01;
end

if SNrGPi == -1 % Substantia nigra inhibits the GPi
        bound = bound - 0.01;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.15 % GPi is excited
        GPiSNr = 0;
        GPiOFC = 0;
else % GPi is inhibited
        GPiSNr = -1; % GPi inhibits the substantia nigra
        GPiOFC = -1; % GPi inhibits the OFC
end
```

```
%Orbitofrontal Cortex Behavior
function [OFCTh, OFCACC, OFCAm, OFCVTA, OFCNAc, OFCOFC, probability] = OFC(ThOFC, AmOFC, VTAOFC, SNrOFC, GPiOFC, OFCOFC, compulsions, trigger)

bound = (0.002 * compulsions) + (0.02 * trigger);

if ThOFC == 1 % Thalamus excites the OFC
        bound = bound + 0.01;
end

if AmOFC == 1 % Amygdala excites the OFC
        bound = bound + 0.01;
end

if VTAOFC == 1 % VTA excites the OFC
        bound = bound + 0.005;
end

if SNrOFC == -1 % Substantia nigra inhibits the OFC
        bound = bound - 0.01;
end

if GPiOFC == -1 % GPi inhibits the OFC
        bound = bound - 0.01;
end

if OFCOFC == -1 % OFC inhibits itself
        bound = bound - 0.02;
end

probability = bound + (1 - bound).*rand;

if probability >= 0.75 % OFC is highly excited
        OFCTh = 1;
        OFCACC = 1;
        OFCAm = 0;
        OFCVTA = 1;
        OFCNAc = 2; %OFC highly excites the nucleus accumbens
        OFCOFC = 0;
elseif probability >= 0.375 % OFC is excited
        OFCTh = 1; % OFC excites the thalamus
        OFCACC = 1; % OFC excites the ACC
        OFCAm = 0;
        OFCVTA = 1; % OFC excites the VTA
        OFCNAc = 1; % OFC excites the nucleus accumbens
        OFCOFC = 0;
else % OFC is unexcited
        OFCTh = 0;
```

```
        OFCACC = 0;
        OFCAm = -1; % OFC inhibits the amygdala
        OFCVTA = 0;
        OFCNAc = 0;
        OFCOFC = -1; % OFC inhibits itself
end
```

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ABOUT THE AUTHOR

Lindsay D. Fields was born in Jacksonville, FL on August 16th, 1993, the eldest of four children. She was a member of the Girl Scouts of America for 13 years, earning her Silver Award, one of the highest honors awarded to a girl scout. Ms. Fields graduated from Paxon School for Advanced Studies in 2011 and obtained her Bachelor of Science in Mathematical Sciences from Florida Agricultural and Mechanical University in May 2015.

During her time at Florida A&M, Ms. Fields was involved as a Learning Assistant, helping lower-level mathematics students through tutoring and mentorship, as well as the Vice-President of the Student Pride Union. She participated in the 2nd Annual STEM Day, which focused on recruiting minority middle- and high-school students into fields involving science, technology, engineering, and mathematics.

Besides her organizational experiences, Ms. Fields has developed her brand as a game theorist with over 7 years of experience in mathematics, economics, and physical sciences. Her research has taken her to Texas, Colorado, and Japan.