A Look at Structural Abnormalities and Symptom Severity in Adolescents with Obsessive-Compulsive Disorder

Sarah Campbell

University of Minnesota

Mentor: Bonnie Klimes – Dougan Ph.D.

Gail A. Bernstein M.D.

Schmuel Lissek Ph.D.

Abstract

The objective of this research was to explore the volumetric differences between OCD and control participants in the cortico-striatal-thalamic-cortico (CSTC) circuit. Functional magnetic resonance imaging (fMRI) was obtained with the Human Connectome Project scanner using newly developed technologies. Seventeen OCD and 13 healthy control adolescents were scanned with the 3T scanner. Freesurfer technology was used to analyze the volumetric findings of the CSTC regions. The thalamic and striatal volume results were analyzed. Adolescents with OCD compared with controls showed no difference in the volumes of the thalamus, caudate and putamen. A significant difference was found between medication naïve and medicated OCD participants in the right putamen. No difference in volumetric regions of the CSTC between OCD and control participants suggests that connectivity may not be related to volumes of the involved regions.

A Look at Structural Abnormalities and Symptom Severity in Adolescents with Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) is an impairing anxiety disorder that affects all ages. Those affected suffer from persistent, unreasonable thoughts (obsessions), and repetitive behaviors (compulsions). Recent neuroimaging studies show an association between OCD and dysfunction in the cortico-striatal-thalamic-cortical circuit (CSTC) (Kalra & Swedo, 2009). Researchers hypothesize that there are brain structural abnormalities within this circuit that correspond to the severity of obsessive thoughts and compulsive behaviors.

The cortico-striatal-thalamic-cortical circuit is a key neural network implicated in OCD. This circuit connects neurons in the frontal cortex, the striatum (putamen and caudate), the thalamus, and back to the frontal cortex. In OCD, it is believed that neurons in the frontal cortex send an excitatory signal to the striatum. This increases the signaling from the striatum to the next node, which is the globus pallidus internus and substantia nigra (GPi/SNr). Since the connection between the striatum and GPi/SNr is inhibitory, an increase in striatal stimulation leads to an increase in inhibition at the GPi/SNr. The next part of the circuit involves an inhibitory signal to the thalamus. This inhibitory signal decreases the amount of GABA, an inhibitory neurotransmitter. This leads to an excitatory signal from the thalamus to the frontal cortex, which is believed to be involved in obsessive thoughts and compulsive actions.

This circuit in the brain can be measured using an fMRI and recording the connectivity between the varying regions in the circuit. In this research, hyperconnectivity refers to a greater strength of connections whereas hypoconnectivity refers to a lower

strength of connections compared to the average. It is hypothesized that when this connectivity is measured using a resting state MRI (R-fMRI), the measured connections can reflect the structural architecture of the brain (volume, thickness) (van den Heuvel, Mandl & Hulshoff, 2009). Interpretation of what hyperactivation or hypoactivation in the brain means in terms of volume is scarce in the literature. A common view is that hypoactivation in the brain is thought to be a neuronal deficit, which can sometimes lead to hyperactivation as a compensatory mechanism and an enlargement of structures (Harrison et al., 2009). Others believe that hyperactivation could be stress-related excitotoxicity, thus decreasing the volume of certain structures (Suzuki et al., 2012).

Emerging research supports the involvement of the CSTC circuit and volumetric abnormalities within the involved regions in adults with OCD. Specifically, recent research has focused on striatal and thalamic volume differences with OCD adults. Christian et al. (2008) presented data supporting the association between the circuit and adult OCD participants. OCD participants demonstrated more gray matter in the left thalamus. Christian speculated that the increase in grey matter could reflect a compensatory mechanism or a neuronal hypertrophy resulting from a neuronal deficit. Further evidence points to a connection between changing striatal volumes and OCD, though this has met with conflicting results. Robinson et al. (1995) looked at 26 adult OCD participants and 26 matched controls. This team found a reduced caudate volume in OCD participants versus control. This team focused on adult patients who had had prior treatment with psychotropic drugs such as selective serotonin reuptake inhibitors (SSRIs) or benzodiazepines. Szesko et al (2004) looked at 23 drug naïve OCD patients and 27 healthy

volunteers. They found no difference in the volumes of the caudate nucleus or putamen, but found smaller globus pallidus volumes.

Similar volumetric findings in children and adolescents with OCD have been found. Gilbert et al. (2000) measured neuroanatomical changes in the thalamus of 21 drug naïve children and adolescents with OCD and 21 age and gender matched controls. They found that thalamic volumes were significantly greater in OCD treatment naïve patients compared to controls, but after 12 weeks of paroxetine treatment, there was a significant decrease in thalamic volume. Rosenberg et al (1997) found similar striatal results to Robinson et al. (1995) but in adolescents and children. Robinson looked at 19 drug naïve children and adolescents and 19 gender and age matched healthy controls. The OCD participants had significantly smaller overall striatal volumes. Specifically, smaller putamen volumes were observed with no change in caudate volumes. The differing findings in striatal volumes in adolescents and children versus adults could be due to developmental factors or treatment effects (medication or cognitive-behavioral therapy).

Furthermore, there is evidence that OCD symptom severity is correlated with volume changes in the brain in both adults and children. In Christian et al (2008), there was a positive correlation between gray matter in the left orbitofrontal cortex and symptom severity. Gilbert found that after the 12 weeks of paroxetine treatment, the OCD symptom severity had decreased with the thalamic volume. Both Christian and Gilbert used the Y-BOCS/CY-BOCS assessment when interviewing their participants.

The current research is sparse in connecting brain connectivity activation to volumetric findings; and little research exists that reports on connectivity and volumetric findings of the same participants. Central to this study are the findings from Bernstein et al.

(2013, in progress). With the current sample they examined the CSTC circuit in OCD and adolescent control participants. Using fMRI they found that a lower level of connectivity, hypoactivation, was found in OCD participants. Because hypoactivtion was observed, one could expect to find lower volumes in the CSTC circuit regions resulting from some type of deficit. The current study aims to look at volumes of the thalamus and striatum in the CSTC and consider if these brain volumes are related to severity of OCD.

Method

Participants

Seventeen OCD participants, ages 12-19, and 13 age- and gender- matched healthy controls were enrolled. All OCD participants (males=9, females=8) met DSM-IV criteria on the Anxiety Disorders Interview Schedule for DSM-IV (ADIS) (an interference rating of at least a 4) and CY-BOCS (overall severity rating > 15). Controls (males=8, females=7) had no psychiatric disorders and had no family history of OCD. Exclusion criteria included the following; autism, psychosis, bipolar disorder, major depression, and substance use disorders on the ADIS; mental retardation on the WASI (IQ<80), Positive urine drug screen done before the scan, MRI incompatible features (see Appendix B); currently pregnant, any anxiolytics outside of SSRI's, anyone outside of the 12-19 age range.

Recruitment

Participants were recruited from the Child and Adolescent Anxiety Disorders Clinic at the University of Minnesota Fairview Medical Center. E-mails with recruitment information were sent to mental health providers and pediatricians in the Minneapolis/St. Paul metropolitan area (Appendix A). We also advertised in local newspapers, Craig's List, and

Facebook. Additional participants were recruited via posters in the community and in clinics.

Procedure

Parents of prospective participants were first interviewed using a phone screen, which included basic questions that would eliminate any participants from the study who met exclusionary criteria (see Appendix C). If participants met the inclusionary criteria, they were invited in for two in-person assessments: an interview and an MRI. During the in-person interview portion of the study, participants and their guardians were given a brief overview of the study and written informed consent and assent were obtained. A 2-3 hour interview followed where assessment instruments, such as interviews and rating scales as described in the Assessments section, were administered by trained researchers. Participants meeting inclusion criteria based on the interview portion underwent an MRI scan at the Center for Magnetic Resonance Imaging at the University of Minnesota. Families were offered $30 for completion of the diagnostic assessment and $35 for the imaging studies. During the second appointment, participants completed a one-hour MRI scan. At the start of the appointment, participants completed the safety screening form in the lobby of the CMRR to ensure that no metal was present on the participant (see appendix). Pre-scan procedures included a urine sample for drug screening and (if female) pregnancy testing at the CMRR. Participants' height, weight, and head circumference were also taken for scanning purposes. Participants were offered the use of a 'mock scanner' before going into the actual scanner to ensure that they were comfortable and ready for the

scan. To obtain the resting state MRI, participants were asked to rest and stay awake with eyes closed and to "not think about anything in particular."

Assessments

Assessments were used to determine exclusionary comorbid disorders. The Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) (Scahill et al., 1997), was used to determine the severity of individual obsessions and compulsions. The CY-BOCS is a modified version of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), which is used for adults. The overall structure of the Y-BOCS assessment was retained but the wording was changed to fit children and adolescents understanding. The researchers used the composite score to determine overall severity. The CY-BOCS was administered with both the parent and the participant present. The Wechsler Abbreviated Scale of Intelligence (WASI), adopted from Wechsler (1999), was used to provide a measure of cognitive functioning. The WASI ensured that each participant's IQ was greater than 79 to rule out any mental retardation. The Beck Depression Inventory (BDI), adopted from Beck (1996), was given tomeasure the severity of depression symptoms. Basic information obtained from participants included demographic information about place of residence, occupation (for Social Economic Status (SES) information), and contact information. The Family Interview for Genetic Studies (FIGS) was given to the participants' guardians to obtain family history of mental disorders. Researchers were each trained in on how to appropriately administer the instruments. Any ambiguous findings were discussed during team meetings with psychiatrists present. Participants were compensated $30 for part one and were asked to sign a reimbursement form. At the end of the interview portion,

participants were sent home with an "MRI experience form" that highlighted what it was like to be in an MRI scanner.

MRI:

Imaging was conducted on a 3T scanner using a 32-channel receive only head coil. This scanner is a new, state-of-the-art Siemens scanner named the SKYRA. The SKYRA uses updated technology to view white matter microstructure. This scanner is also being utilized on the Human Connectome project, a recent initiative to map the human brain. Whole brain anatomical data with T1 contrast were acquired in 5 minutes using an MP-RAGE sequence with 1 mm isotropic resolution (TR = 2530 ms, TE = .52 ms, TI = 1100 ms, flip angle = 7 degrees). The T1 images were processed using FreeSurfer (http://surfer.nmr.mgh.harvard.edu/). Specific FreeSurfer ROIs for each structure within CSTC were identified and later aligned to functional images.

Design

In a between-subjects design, participants were recruited based on having OCD or being a healthy control. Measurements using a resting state MRI were made to see if brain structure differed between OCD/control participants.

Results

Participants:

Demographic information and severity scores on the given assessments between the OCD and control groups can be seen in Table 1. There were no significant differences between

the groups on socioeconomic status, age at assessment, gender, ethnicity or handedness. Twelve of the 15 total OCD participants were on an SSRI and/or clomipramine to manage their OCD. The mean score on the CY – BOCS for the OCD group was a 19.3, indicating that the average level of OCD severity was moderate.

Volumetric Results:

OCD versus control groups were compared on three bilateral brain regions. A multivariate analysis of variance (MANOVA) was run on the six brain regions between groups. There was a main group effect of 0.697. Intracranial brain volume was used as a covariate to remove its relationship from the volumetric findings. There were no significant differences between OCD participants and control participants (Table 2). Although not significant, larger volumes were found in the OCD group in the right and left thalamus, right and left caudate, and right putamen (figure 1). The volumes between medication naïve and medicated OCD participants (n=14 naïve, n=3 medicated) was ran with a significant difference ($p = .005$) in the volume of the right putamen.

Association of Volumes with OCD Severity:

Pearson correlation coefficients were run to evaluate if the volumetric data were significantly related to the severity on the CY–BOCS in the OCD group. The CY-BOCS total score, the total obsessions score, and the total compulsions score were ran versus the six brain regions. As seen in Table 3, no significant differences were found.

Discussion

Our study replicates earlier adult studies that show no significant differences in the striatum between OCD and control participants (Szesko et al., 2004). Our study did not find any differences in the thalamic volumes between OCD and control participants contrary to two previous studies done in adolescents that found an increase in thalamic volume (Christian et al. 2009; Gilbert et al. 2012). A significant difference was found between medication naïve and medicated OCD participants in the volume of the right putamen ($p = .005$); with a smaller volume being found in the OCD participants' striatum. Because of the small sample size of medication naïve participants ($n=3$), this significance is not conclusive. There was no significance found on the left putamen.

A number of conclusions can be drawn from this experiment. The first is that although there seem to be differences in connectivity between OCD and controls, there may not be volumetric differences between the two. Further research into the CSTC circuit and other brain regions is needed to ensure that the volumetric differences between these groups does not exist. In future studies, researchers should look specifically at medication naïve, severe OCD patients. Researchers could try manipulating the CSTC in different ways and look to see how the obsessions and compulsions are affected. The second conclusion that can be drawn is that connectivity may not be related to the volumes of the involved regions. While connectivity is a relatively new area of understanding, more research will need to be done to see how the connectivity relates to the affected areas. Future research may uncover whether hypoconnectivitt/hyperconnectivity means the growth of less/more white matter or simply a weaker/stronger electrical signal. The third conclusion is that there is hope for sufferers of OCD. Many methods, such as deep brain stimulation and brain lesions, can be done to certain areas of the brain to try to subdue the symptoms. Also,

because researchers now have a specific area to focus on, medication that targets specific neurotransmitter abnormalities may be developed in the future.

Future directions for this research include trying to find distinct differences between child, adolescent, and adult OCD volumetric abnormalities. It is believed that the symptoms of OCD change as one gets older, and so might the connections in the brain, leading to differences in brain volumes. Because OCD commonly emerges during childhood or adolescence, it is possible that it is altering neurodevelopment in some way. Fitzgerald et al. (2011) investigated if connectivity in the CSTC circuit was distinguishable between OCD and controls in four developmental age groups: children, adolescents, young adults and older adults. This group found reduced connectivity in specific connections between regions of the CSTC in children with OCD; and increased connectivity across all age groups in other CSTC connections. Although their results are informative in how the connectivity of the CSTC circuit develops with OCD, there were a number of confounding explanations for their findings as well. This difference in circuitry between children and adulthood could be environmental as well as genetic. Fitzgerald et al. (2011) performed a cross-sectional design; whereas future research should be done with a longitudinal design to account for brain changes over time. As with all psychiatric disorders, researchers will continue to look for a biological basis which enables us to quantify differences in behaviors and link them to specific brain regions.

There are several shortcomings of this study that could have lead to negative findings. First of all, the sample size in Bernstein et al. (2013, in progress) was small. This pilot study used two 12-minute recordings of resting-state functional connectivity. This is an advantage in collecting data, but is a disadvantage in acquiring numerous participants.

One subject's data could not be analyzed because of motion in the scanner. This small sample size also likely affected the correlations made between the CY-BOCS and volumetric data. Furthermore, inclusion criteria required CY-BOCS total score >15. The narrow range of scores in this study may have impacted/reduced the likelihood of finding significant correlations between volume and OCD severity. Another shortcoming of this study was that most of the patients were on medications, which may have normalized any volumetric differences that were present before medications. Bernstein et al. (2013) found that the connectivity patterns in the brain were not static, but were changing over the 24 minutes of data collection. Medication could have a dramatic impact on the strength of these connections being made and the effects these connections have on the architecture of the brain. Future studies should follow a before and after treatment model (similar to Gilbert et al. 2000) to perform studies of this nature.

References

Bernstein, G.A., Mueller, B.A., Campbell, S.M., Regan, E., Yacoub, E., Lee, S.S., Westlund, M.K., Houri, A.K., Nelson, P.M., Lim, K.O., Ugurbil, K., Cullen, K.R. (2013). In progress.

Christianson, C J., Lencz, T., Robinson, D. G., Burdick, K. E., Ashtari, M., Malhotra, A. K., Betensky, J. D., & Szeszko, R. (2008). Gray matter structural alterations in obsessive-compulsive disorder: Relationship to neuropsychological functions. *Journal of Psychiatric Research: Neuroimaging, 164,* 123-131. doi:10.1016/j.pscychresns.2008.03.005

Components of the Human Connectome Project. (2011). Retrieved October 1, 2011 from http://humanconnectome.org/about/project/HARDI-acquisition.html

Fitzgerald, K. D., Welsh, R. C., Stern, E. R., Angstadt, M., Hanna, G. L., Abelson, J. L., & Taylor, S. F. (2011). Developmental alterations of frontal-striatal-thalamic connectivity in obsessive compulsive disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 50,* 938-948. doi:10.1016/j.jaac.2011.06.011

Gilbert, A.R., Moore, G.J., Keshavan, M.S., Paulson, L.A., Narula, V., Mac Master, F.P., Stewart, C.M., & Rosenberg, D.R. (2000). Decrease in thalamic volumes of pediatric patients with obsessive-compulsive disorder who are taking paroxetine. *Arch General Psychiatry, 57(5), 449-56.*

Harrison, B.J., Soriano-Mas, C., Pujol, J., Ortiz, H., Lopez-Sola, M.m Hernandez-Ribas, R., Deus, J., Alonso, P., Yucel, M., Pantelis, C., Menchon, J.M., & Cardoner, N. (2009). Altered cortciostriatal functional connectivity in obsessive-compulsive disorder. *Arch General Psychiatry, 66, 1189-200.* doi: 10.1001/archgenpsychiatry.2009.152

Kalra, S., & Swedo, S. (2009). Children with obsessive-compulsive disorder: Are they just "little adults"? *Journal of Clinical Investigation, 119,* 737- 746. doi:10.1172/JCI37563

Robinson, D., Wu, H., Munne, R.A., Ashtari, M., Alvir, J.M., Lerner, G., Koreen, A., Cole, K., & Bogerts, B. (1995). Reduced caudate nucleus volume in obsessive-compulsive disorder. *Arch Gen Psychiatry*, *52(5), 393-8.*

Rosenberg, D.R., Keshavan, M.S., O'Hearn, K.M., Dick, E.L., Bagwell, W.W., Seymour, A.B., Montrose, D.M., Pierri, J.N., & Birmaher, B. (1997). Frontostriatal measurement in treatment-naïve children with obsessive-compulsive disorder. *Arch Gen Psychiatry, 54(9), 824-30.*

Scahill, L., Riddle, M.A., McSwiggin-Hardin, M., Ort, S.I., King, R.A., Goodman, W.K., Cicchetti, D., & Leckman, J.F. (1997). Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. *Journal of the American Academy of Child and Adolescent Psychiatry, 36(6), 844-52.*

Suzuki, H., Botteron, K.N., Luby, J.L., Belden, A.C., Gaffrey, M.S., Babb, C.M., Nishino, T., Miller, M.I., Ratnanther, J.T., & Barch, D.M. (2013). Structural-functional correlations between hippocampal volume and cortico-limbic emotional responses in depressed children. *Cognitive Affect Behavioral Neuroscience, 13(1), 135-51.* doi: 10.3758/s13415-012-0121-y

Szeszko ,P.R., MacMillan, S., McMeniman, M., Chen, S., Baribault, K., Lim, K.O., Ivey, J., Rose, M., Banerjee, S.P., Bhandari, R., Moore, G.J., & Rosenberg, D.R. (2004). Brain structural abnormalities in psychotropic drug-naïve pediatric patients with obsessive-compulsive disorder. *American Journal of Psychiatry, 161(6), 1049-56.*

Van den Heuvel, M.P., Madl, R.C., Kahn, R.S., Hulshoff Pol, H.E. (2009). Functionally linked resting-state networks reflect the underlying structural connectivity architecture of the human brain. *Human Brain Mapp, 10, 3127-41.* doi: 10.1002/hbm.20737

Table 1. Demographics and Severity Scores

	OCD (n = 16)[a]		Control (n = 13)		Significance Test	p
Age at onset,[b] mean (SD)	9.3	(3.9)	N/A			
Age at assessment, mean (SD)	15.3	(2.0)	16.0	(1.8)	t = 0.93	0.36
Gender, n (%)					χ^2 = 0.90	
Male	9	(59)	6	(46)		
Female	7	(41)	7	(54)		
SES, mean (SD)	53.4	(7.4)	50.0	(16.7)	t = -0.72	0.12
WASI IQ, mean (SD)	115.3	(11.2)	108.3	(15.0)	t = -1.41	0.17
Ethnicity, n (%)					χ^2 = 0.34	
Caucasian	14	(88%)	8	(61.5%)		
Latino	1	(6%)	3	(23.1%)		
Asian	1	(6%)	2	(15.4%)		
1st-degree family history of OCD, n (%)						
Yes	6	(40%)	0	(0%)		
No	7	(47%)	12	(100%)		
Unknown	2	(13%)	N/A			
Handedness, n (%)					χ^2 = 0.255	
Right	15	(94)	11	(92)		
Left	1	(6)	1	(8)		
Current medications, n (%)						
SSRI or clomipramine	8	(53.3%)	0	(0%)		
SSRI and/or clomipramine + other psychotropic medication(s)	4	(26.7%)	0	(0%)		
Medication-Free	3	(20%)	12	(100%)		
Current comorbidity, n (%)						
Tic disorder	3	(18%)	0	(0%)		

Social phobia	4	(24%)	0	(0%)		
ADHD	3	(19%)	0	(0%)		
ODD	2	(12%)	1	(6%)		
MDD	1	(6%)	0	(0%)		
Severity Scores						
CY-BOCS, mean (SD)						
Total	19.3	(3.7)	0.1	(0.3)	t = -18.6	0.00
Obsessions	9.3	(2.2)	0.1	(0.3)	t = -14.7	0.00
Compulsions	10.1	(1.8)	0.0	(0.0)	t = -20.0	0.00
BDI, mean (SD)	9.4[c]	(9.3)	1.3	(2.8)	t = -3.02	0.01
COIS-R, mean (SD)						
Child	18.6[d]	(9.4)	0.7	(2.2)	t = -6.7	0.00
(possible range = 0-99)						
Parent	31.9[e]	(22.3)	0.1	(0.3)	t = -5.1	0.00
(possible range = 0-99)						
YGTSS, mean (SD)						
Total	3.0	(7.0)	0.0	(0.0)	t = -1.5	0.14

[a] 1 subject did not finish scan and 1 excluded from all analyses due to scrubbing process

[b] based on parent report if available, otherwise adolescent report

[c] missing data on 5 subjects

[d] missing data on 2 subjects

[e] missing data on 3 subjects

Table 2.

Volumetric Results

Region	**OCD n = 16**	**Control n = 13**	**Between Subjects Effect**
Left Thalamus	7980.9 (758.8)	7863.62 (626.9)	p = .557
Left Caudate	4434.0 (562.8)	4347.8 (662.5)	p = .774
Left Putamen	6663.3 (639.3)	6717.5 (858.5)	p = .325
Right Thalamus	7980.0 (766.5)	7776.9 (801.2)	p = .865
Right Caudate	4624.1 (578.0)	4409.5 (786.7)	p = .811
Right Putamen	6530.4 (588.8)	6368.9 (830.6)	p = .902

Note: Main effect p = .697

Table 3.

Severity Results

Region	**CY – BOCS Obsessions**	**CY – BOCS Compulsions**	**CY – BOCS Total**
	p (Correlation)	p (Correlation)	p (Correlation)
Left Thalamus	.802 (.05)	.763 (.06)	.780 (.06)
Left Caudate	.731 (.07)	.882 (.03)	.807 (.05)
Left Putamen	.776 (-.06)	.682 (-.08)	.725 (-.07)
Right Thalamus	.729 (.07)	.702 (.08)	.712 (.07)
Right Caudate	.572 (.11)	.640 (.09)	.604 (.10)
Right Putamen	.461 (.15)	.382 (.10)	.532 (.12)

Note: A Pearson Correlation was ran.

Figure 1.

Trend in volumetric findings.

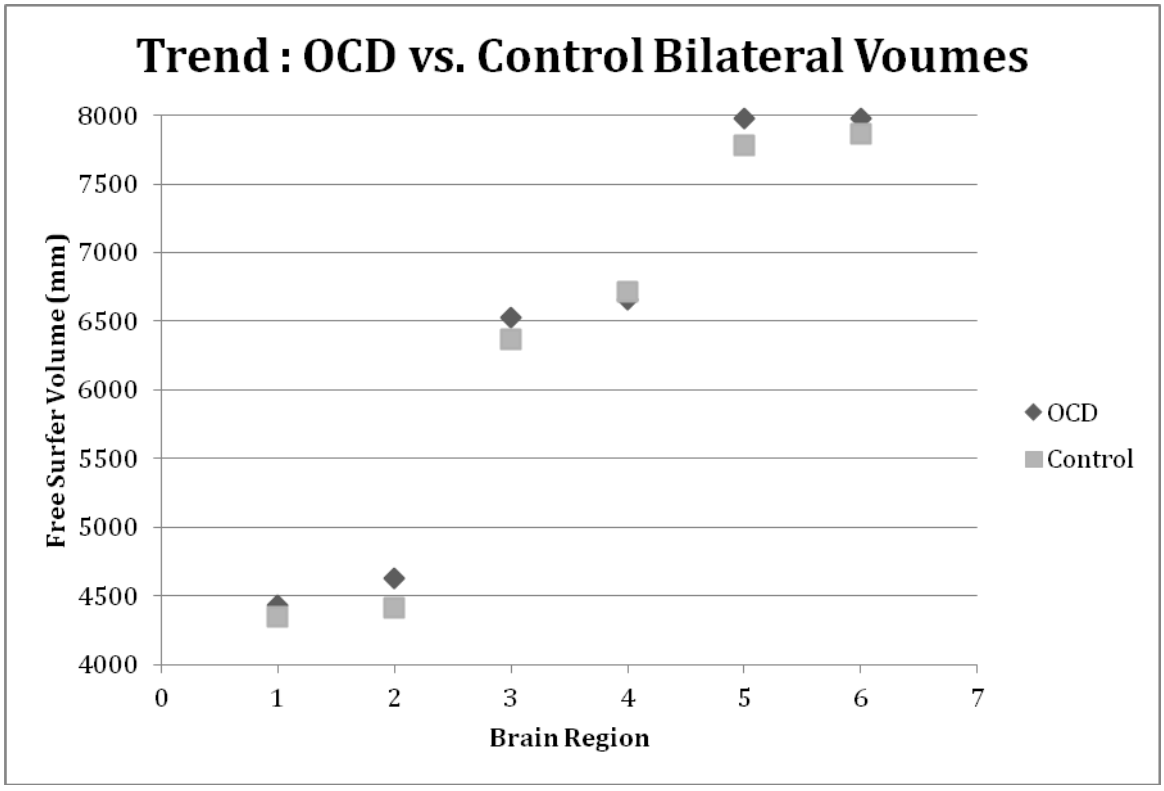

Figure 1: Figure 1 shows the trend of specific brain region volumes in OCD participants versus OCD participants. Brain regions: 1 = Left caudate; 2 = Right caudate; 3 = Right putamen; 4 = Left putamen; 5 = Right thalamus; 6 = Left thalamus

Appendix A

Do You Have a Teenager with Obsessive-Compulsive Disorder?

If you have a teenager who is 13-17 years old with Obsessive-Compulsive Disorder (OCD), he or she may be eligible to participate in a research study at the University of Minnesota. We are recruiting adolescents with OCD and healthy controls for a study of brain imaging of youth with OCD. **Participants will be compensated for their time and contributions.** If you have a teenager who might be interested in this research opportunity, please contact **Dr. Gail Bernstein at 612-273-9711 or her research assistants at 612-273-9743.**

Appendix B

Name:_____ Date:_____ DOB: _____ (mm/dd/yy) Weight: ____lbs

For staff only:		
Session #:	IRB #:	Operator #:

CMRR Safety Screening Form

1. Do you have a problem with claustrophobia (fear of closed spaces?)
   No_____ A little _____ Pretty much _____ Severe _____

2. Do you have a heart pacemaker or defibrillator or other implanted devices?
   No _____ Yes _____

3. Have you ever had an operation? If yes, Investigator to fill out Page 2.
   No _____ Yes _____

4. Have you ever been injured by metallic foreign body which was not removed?
   No _____ Yes _____

5. Do you wear braces on your teeth? Do you have removable bridgework or false teeth?
   No _____ Yes _____

6. Do you have any tattoos or unremovable body piercings? If so, indicate where.
   No _____ Yes _____

7. Do you wear a hearing aid? If yes, it will need to be removed for the scan.
   No _____ Yes _____

8. (Females only): *It is recommended that you not wear underwire bras for the scanning session, due to possible discomfort when the metal is attracted by the field, and a small risk of heating in the wire.*
   Do you have any reason to believe that you are pregnant? No _____ Yes _____
   Are you currently using (wearing) an IUD or diaphragm? No _____ Yes _____

9. Please list medications you took today or are taking regularly.
   (try to include the name of the medicine, dose, how often, and time of last dose).

10. Have you ever had any previous studies (MRI, CT or other)? If yes circle on list.
    No _____ Yes _____

11. Do you have a breathing disorder or movement disorder? If yes describe.
    No _____ Yes _____

_____ Date:_____/_____/_____
Signature of Person Completing Page 1

Investigator to complete if Item #3 on Page 1 is Yes.

Some of the following items may be hazardous to your safety and some can interfere with the MRI examination. Please check the correct answer for each of the following. Do you have any of the following:

Yes	No	Cardiac pacemaker
Yes	No	Implanted cardiac defibrillator
Yes	No	Carotid artery vascular clamp
Yes	No	Intravascular stents, filters, or coils
Yes	No	Aortic clip
Yes	No	Internal pacing wires
Yes	No	Vascular access port and/or catheter
Yes	No	Swan-Ganz catheter
Yes	No	Shunt (spinal or intraventricular)
Yes	No	Aneurysm clip(s)
Yes	No	Neurostimulator
Yes	No	Electrodes (on body, head, or brain)
Yes	No	Heart valve prosthesis
Yes	No	Any type of prosthesis (eye, penile, etc.)
Yes	No	Artificial limb or joint replacement
Yes	No	Bone growth/fusion stimulator
Yes	No	Bone/joint pin, screw, nail, wire, plate
Yes	No	Metal rods in bones
Yes	No	Harrington rods (spine)
Yes	No	Metal or wire mesh implants
Yes	No	Wire sutures or surgical staples
Yes	No	Insulin pump or infusion device
Yes	No	Transdermal delivery system (Birth Control/Nicotine/Nitro)
Yes	No	Any implant held in place by a magnet
Yes	No	Cochlear, otologic, or ear implant

NOTE: YOU ARE REQUIRED TO WEAR EARPLUGS OR EARPHONES DURING THE MRI EXAMINATION.

_____ Date:____/____/____

Signature of Investigator Completing Page 2

Appendix C

Telephone Screening Form

Exploring Brain Connectivity in Youth with Obsessive-Compulsive Disorder

Date:_____

Source (check one) Outpatient Inpatient Advertisement Other

(If advertisement, pleases specify where it was seen:_____)

(If other, please specify: _____)

Screen completed by: _____

Child's name:_____ Sex:_____

Handedness (check one) Left Right Both

Race/Ethnicity: (check all that apply)

Hispanic or Latino_____

American Indian/Alaskan Native_____

White_____

Black or African-American_____

Native Hawaiian or Other Pacific Islander_____

Asian_____

Other_____

DOB:_____ Age:____

School:_____ Grade:_____

Parent/Guardian's name(s): _____

Address:

_____

_____

Email: _____

Home phone:_____ Work phone:_____ Cell phone: _____

☐ Can leave message ☐ Can leave message ☐ Can leave message

Has your child ever been diagnosed with OCD?

_____

_____

What are your current observations that suggest OCD in your child?

_____

_____

Has your child ever been diagnosed with major depression?

_____

_____

Has your child ever been diagnosed with bipolar disorder?

_____

_____

Has your child ever been diagnosed with schizophrenia or psychosis?

_____

_____

Has your child been diagnosed with autism, Asperger's disorder, or pervasive developmental disorder?

_____

_____

Does your child have a history of substance use or chemical dependency treatment? If so, which drugs were used? Is this a current issue?

_____

_____

****If potential subject has a positive urine drug screen, he/she will not have the MRI.****

Current/Past Medications. For current medications, please indicate when the medications were started.

Medical History. Was your child premature? Is there a history of any chronic illness such as cerebral palsy, diabetes, heart disease, or cancer? Is there a history of serious accidents or head injuries? Has there been a history of loss of consciousness? If so, how long did it last?

_____

_____

Treatment. Does your child have a history of psychiatric treatment or hospitalization? For current or recent therapies, list type of therapy and duration.

Family History. Has anyone in the immediate family (child's parents of siblings) been diagnosed with OCD? If so, who? Has anyone in the extended family been diagnosed with OCD? If so, who?

_____

_____

Safety Screening Questions:

1. **Claustrophobia Y N**
2. **History of surgery Y N**
3. **Braces Y N**
4. **Un-removable body piercings Y N**
5. **Tattoos Y N**
6. **Implanted Devices Y N**

****If potential participant could be pregnant, she will not have the MRI.****