

# In the Loop

The Yale Child Study Center Tourette Syndrome and  
Obsessive-Compulsive Disorder Research Team Newsletter

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## TS/OCD Research Highlights - 2011

This issue of In the Loop features studies to confirm and expand treatment options for children with Obsessive Compulsive Disorder (OCD) and Pediatric Autoimmune Neuropsychiatric Disorders Associated with Strep (PANDAS) (Williams, Swedo interview), others that provide practical guidance for parents dealing with children with OCD (Lebowitz), and an exciting new look at the relationship between OCD and attachment (Gordon). Next, we consider the lifetime arc of Tourette Syndrome (TS) symptomatology with a look at tic severity issues in early childhood that may be predictive of future outcome (Bloch), and further explore the relationship between TS and ADHD (Sukhodolsky). We also present novel and engaging treatment possibilities for TS (Hampson, Kobets) as well as a fascinating study that is underway to assess the creativity of children and adolescents with TS (Zanaboni).

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### Announcement

We are proud to announce that Michael Bloch M.D., M.S. has been appointed to the Yale Medical School faculty as an Assistant Professor. He has received an NIMH career development award to follow up TS subjects in early adulthood that had been previously evaluated as children at the Child Study Center.

### New Grants

Late breaking news includes continued support from the National Institute of Mental Health (NIMH) for: 1) genetic studies under the leadership of Matthew State M.D., Ph.D. and 2) funding to continue a Bench-to-Bedside grant awarded to Drs. Leckman and Swedo that is discussed in the lead article interview.

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## Talking about IVIG Treatment for OCD Children with PANDAS

*Recently Kyle Williams, M.D., spoke with Sue Swedo, M.D. at the National Institute of Mental Health about the joint Bench-to-Bedside Yale/NIMH study that was recently initiated. The study focuses on a relatively rare form of OCD that has an "overnight" onset (PANDAS) and that can be treated with "immunomodulatory" interventions such as IVIG. As part of this same study, Dr. Williams received a grant from the International OCD Foundation to study the immune systems of these children before and after IVIG treatment.*



Susan E. Swedo, M.D.  
Chief, Pediatrics &  
Developmental  
Neuroscience Branch,  
NIMH

**KW:** Dr. Swedo, would you please define PANDAS and IVIG?

**Dr. Swedo:** PANDAS stands for Pediatric Autoimmune Neuropsychiatric Disorders Associated with

(Continued on page 2)

Streptococcal infections and is currently defined by the following clinical features: abrupt, dramatic “overnight” onset of OCD; prepubertal symptom onset; concurrent acute onset of additional neuropsychiatric symptoms that may include separation anxiety, emotional lability, irritability, atypical aggressiveness, behavioral regression, problems with school performance, and/or sensory or motor abnormalities (including tics); and temporal association between symptomatic periods and infections with Group A Strep, i.e. “Strep Throat.” IVIG stands for intravenous immunoglobulins, a medical term that describes delivering a large amount of antibodies (collected from donors during blood transfusions) to an individual through an intravenous line.

**KW:** Would you tell us something about your earlier investigation of PANDAS treatments?

**Dr. Swedo:** IVIG, along with another autoimmune therapy called plasma exchange, was used in a study conducted at the NIMH in the late 90’s. Children with OCD were split into three groups: one group received IVIG and another received placebo (blinded administrations) while the third group was treated with an unblinded series of plasma exchanges. The group that received IVIG showed a 45% reduction in the severity of their OCD symptoms one month after treatment, and these improvements were maintained one year after treatment. The plasma exchange

group also showed strong improvements in their OCD symptom severity (58% decreased) and tic symptom severity (49% decrease), while the placebo group showed no improvement (these children were then offered IVIG or Plasma Exchange therapy, and subsequently showed similar improvements to the IVIG and Plasma Exchange groups). While this study demonstrated that IVIG and Plasma Exchange are both effective therapies for the OCD and tic symptoms seen in PANDAS children, IVIG

is a more readily available treatment and less “invasive” in that it does not require placement of a special IV, termed a “central line.” For these reasons, we have chosen to focus on IVIG in the current treatment trial of PANDAS.

**KW:** Yes, let’s hear more about the study that’s going on now.

**Dr. Swedo:** The current trial is investigating the efficacy of treating PANDAS children with IVIG. It is a collaboration between Yale University and NIMH, with the clinical care provided by physicians in Bethesda and symptom ratings done by the Yale team of investigators. To be eligible for study participation, children must be acutely ill with obsessive-compulsive symptoms, as

well as the accompanying behavioral, emotional and neurological symptoms of PANDAS; and have evidence of a triggering streptococcal infection. Children deemed eligible for study participation are randomly assigned to receive either IVIG or placebo in a “blinded” fashion. For this blinded study, only the NIMH pharmacists will be aware of the nature of the infusion. The investigators, parents and participants won’t know whether the child will receive active IVIG (1 gm/kg/day for two consecutive days), or the sham infusion of an “inert” IV fluid which should not produce improvements in the child’s PANDAS symptoms. Since headache, nausea and vomiting are reported by 20-30% of children who receive IVIG, the investigators were concerned that the side effects might “break the blind” and reveal that the child received active therapy, so all study ratings will be done by the investigators at Yale University via videoconference. The Yale team will not receive information about any side effects that the child experienced during the hospitalization or after discharge. They will assess only the status of the OCD and other PANDAS symptoms. It is hoped that taking this extra step to protect the blinding of the study will yield more definitive results than the earlier study did, which in turn may permit wider acceptance of the benefits of IVIG therapy for children with acute symptoms of PANDAS.



Kyle Williams, M.D.  
Yale Investigative Medicine  
Ph.D. Program  
Yale Child Study Center

**KW:** How does IVIG relate to PANDAS?

**Dr. Swedo:** IVIG is a standard treatment used in a variety of autoimmune disorders in both adults and children, though the way in which it improves autoimmune disorders is not fully understood. We are still in the process of learning what “type” of autoimmune disorder is involved in PANDAS, so it is unclear how IVIG is improving symptoms in PANDAS children. However, we have demonstrated with the 1999 study that IVIG is particularly effective in reducing OCD symptoms in PANDAS children, and are continuing to investigate the mechanism of IVIG’s treatment effect.

**KW:** What are the criteria for entering this study?

**Dr. Swedo:** The criteria include male and female children ages 4-12 with a primary diagnosis of OCD with or without a tic disorder. The acuity of symptom onset/exacerbation is key and must be severe, dramatic in onset, and proceed from no/minimal symptoms to maximum severity within 24-48 hours. It must be temporally related to Group A Strep infection, and be accompanied by at least 3 symptoms including such issues as increased anxiety, aggression, concentration problems, sleep disorders, motor, or urinary problems. For a full description of study criteria, go to the website *clinicaltri-*

*als.gov*. Follow these prompts: List studies by Condition, Behaviors & Mental Disorders, Obsessive Compulsive Disorder, and then go to study # 138 on the list.

**KW:** If a child is eligible for the study, what happens next?

**Dr. Swedo:** The active study is six months long, but the study team will stay in touch by telephone to obtain follow-up information for the next three years. After a telephone screening, eligible children and their families will be brought to the NIH Clinical Center. Further screening will occur there. If still eligible, children will be admitted to the inpatient unit and will

study team will want to keep in touch with families by phone for three more years after the end of the six-month study.

**KW:** When do you expect to have results?

**Dr. Swedo:** This is largely dependent upon how quickly we can enroll patients who meet criteria into the study. We anticipate the results to be compiled within 3 years, and our recruitment is moving at a brisk pace.

**KW:** Is it a one-shot, or would treatment need to be done a number of times?

**Dr. Swedo:** This depends largely on the clinical improvement seen in the child; the current study is designed to offer two treatments of IVIG, if necessary.

**KW:** What do you predict about long-term outcomes for PANDAS patients after IVIG?

**Dr. Swedo:** The previous 1999 study showed that children whose symptoms improved with IVIG continued to show improvement at one year following treatment. Our goal with this study is to gain a better understanding of how long a child’s improvement in symptoms lasts after IVIG, and thus we will follow-up periodically with children in the study for the next three years. At this point, we are hopeful for long-term gains in children who respond to IVIG treatment, but we are still in the process of answering this important question.

*Our goal with this study is to gain a better understanding of how long a child’s improvement in symptoms lasts after IVIG.*

receive a study drug, IVIG or placebo, over two days. This first study visit will last 4-5 days, and several of the days will be spent in the hospital. After six weeks, the child will return to NIH and repeat some of the tests and evaluations he/she had done at the baseline visit. If the child is better, he/she can go back home the next day. If he/she is not better, the doctors may offer treatment with active IVIG (no placebo). Additional NIH clinic visits will occur 3 months and six months after the first evaluation. The

# A Study to Determine Why Many Children with Tics Improve During Adolescence

Michael Bloch, M.D., M.S.

Roughly one-half to two-thirds of children with Tourette syndrome (TS) have a significant reduction of tic symptoms during adolescence. In fact, one-third to one-half of children with TS experience a complete remission of tic symptoms during adolescence. Tics typically emerge around the age of 4-6 years, reach their worst-ever stage early in the second decade of life and then, on average, improve during adolescence. Individuals with TS that persists into adulthood generally have the most dramatic presentations of the illness that we treat. Coprolalia, self-injurious and severe tics are much more common in adults with tics than kids.

When we treat children with tics in our clinic, it is largely unknown which children's tics will improve by adulthood. Improved and individualized knowledge about long-term prognosis in children with TS would significantly influence our treatment of them. For instance, I would be much less likely to prescribe a medication for tics or advise a family to concentrate on engaging in a behavioral therapy to treat tics



Michael Bloch, M.D., M.S.  
Assistant Professor  
Yale Child Study Center

if I knew the child was likely to get better in the next couple of years anyway. Conversely, I would be much more aggressive in recommending behavioral treatments for tics early on and prescribing medications if I knew the tics were likely to persist.

In order to investigate this issue, we have followed a cohort of 46 children with TS who were originally treated at the Yale Child Study Center prior to age 14, and contacted them again in early adulthood. Eighty-five percent reported a reduction in tic symptoms during adolescence. Only two reported that their adulthood tics were at similar levels compared to childhood. The average age at

Worst-ever OCD symptoms occurred approximately 2 years later than worst-ever tic symptoms. Clinical assessments in childhood were poor predictors of adulthood tic and OCD severity with only the children's level of tics at initial assessment being weakly correlated with adulthood outcome. A child's tic severity at initial assessment explained only about 10% of the variation in adulthood tic severity at adulthood follow-up.

We have additionally examined the association between childhood neuropsychological testing and structural neuroimaging with future tic severity in these children. We found that reduction in the volume of the caudate nucleus in childhood was associated with a persistence of tic symptoms into adulthood. The caudate nucleus

*In order to investigate this issue, we have followed a cohort of 46 children with TS... Eighty-five percent reported a reduction in tic symptoms during adolescence.*

worst-ever tic severity was 10.6 years. Forty-one percent of patients with TS reported having experienced at least moderate OCD symptoms at some point.

is a region of the brain (part of a group of structures called the basal ganglia) that has been demonstrated previously to be reduced in patients with TS compared to healthy controls. The caudate nucleus has also been shown to be central in the pathogenesis of

tics in terms of both tic generation and tic suppression in other neuroimaging studies.

We further found that poor fine-motor skills in childhood, measured with neuropsychological testing, was also associated with the persistence of tics into adulthood. Fine-motor skills were assessed using the Purdue Pegboard Test, in which children are asked to place as many metal pegs in a wooden board with holes as they can in 30 seconds. Fine-motor skills are also believed to be a broad measure of basal ganglia functioning.

Another important question is: Why do the tics improve in some children and not others? Are there adaptations in some children's brains during adolescence that make them better able to suppress tics and reduce premonitory urges? To address this question we have received additional funding to reevaluate these children using MRI and neuropsychological testing now that they are adults. Comparing the brain changes in subjects whose tics remitted compared to those whose tics persisted will allow us to potentially uncover compensatory

changes in the brain that may help tics improve. This comparison may also help us understand the consequences of having years of persistent tics (if there are any). Understanding compensatory brain mechanisms that reduce tics (1) will help us better understand TS, (2) may help us provide more accurate prognostic information to families and (3) may help us develop better treatments in the future that encourage these pathways. I look forward to sharing these additional results with you as they become available.

### **Transcranial Magnetic Stimulation Study**

Researchers at the Child Study Center are interested in looking more closely at the electrical brain activity related to Obsessive Compulsive Disorder compared to the inhibitory electrical activity present in individuals that are not affected with this condition. This non-invasive study uses a magnet placed on the scalp. The magnet can measure brain activity by stimulating the part of the brain that controls finger movement. Both healthy individuals and people with OCD will participate in this study. For further information please contact: **Maria Motlagh, M.D.**, at [maria.motlagh@yale.edu](mailto:maria.motlagh@yale.edu) or (203) 785-7683.

We would like to express our sincere appreciation to everyone who has contributed to our research program by volunteering for studies and by donations.

Special thanks to  
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Aerin and Eric Zinterhofer, The Rembrandt Foundation,  
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Thank you ALL for your crucial and ongoing support!



## When OCD Takes Over.... The Family!

Eli Lebowitz, Ph.D.

Suffering from OCD is such a heavy burden to bear. There are so many rules you need to follow so as not to feel you are tempting fate or inviting catastrophe. So many things you need do or not to do in order to avoid the anxiety and distress that inevitably continue to pursue you all the same. It is no wonder that many people of all ages who suffer from the disorder



Eli Lebowitz, Ph.D.  
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feel that their life has been “taken over.” OCD can be the ultimate tyrant, forcing you to follow his every whim and always threatening you with the thing you fear the most as the consequence of disobedience.

Anyone familiar with the disorder is aware of just how tyrannical it can be, but recent research is focusing our attention on the ways in which others, alongside the individual with the OCD, can be drawn into the cycle of fear and obedience. As one child put it to me, “What good is it if I wash my hands sixteen times before I eat? After all, Mommy is making the dinner and she didn’t wash her hands!” Indeed, *accommodation* by the family to the child’s OCD has been shown to be more the rule than the exception. Almost all parents who have a child with the disorder will find themselves

adapting to the problem. For some it will be the need to provide constant reassurance, for others avoiding going places that trigger the anxiety, and for some it could be extreme accommodation that completely hinders the entire family’s daily life. Accommodation has not only been shown to be extremely common, it also has serious implications for the course of the disorder, correlating with more severe symptoms and worse outcomes for treatment attempts.

But accommodation is only part of the problem. Like any smart tyrant OCD can make those who fear it into unwilling deputies. For a child suffering from OCD, who feels that her parents’ accommodation is the only way to get through the day, any means may be justified in enforcing the accommodation. In very recent and ongoing studies we are looking at the behaviors that children will employ to ensure their parent’s continued cooperation. Threatened or actual physical violence, outbursts of rage, emotional ‘blackmail’ and dramatic displays of distress are all reported by parents of children who feel they have absolutely no choice but to force their relatives to accommodate.

Among the rules we en-

counter are the insistence that parents complete rituals; prohibitions against making certain sounds or against changes in the home; demands for ritualized cuddling; bans against certain items that arouse disgust like creams or lotions; demands that parents complete feared actions on behalf of the child, and many others. We are not yet sure how common such coercive behaviors are among children with OCD but an as yet unpublished survey would lead us to believe they are very familiar to most experts in the field. In one dramatic example of coercion a child would consistently threaten to kill himself if his parents refused to abide by his rule whereby no windows could ever be opened anywhere in the house for fear of ‘radiation’ seeping in.

So how to manage the coercive behaviors and how do you help an entire family subjugated by one child’s OCD? Clinical experience points to the importance of parent work in creating change in these situations. Often it seems as though the child, unable to stand up to the OCD herself is in need of parental figures that are able to do it for her. As another boy once told me, with his parents out of the room, “I wish they would just say “no!” to me... But don’t tell them because then I’ll feel like it’s my choice after all.”

## Neuropsychological Performance in Children with Tourette Syndrome with and without Co-occurring ADHD

Denis G. Sukhodolsky Ph.D.

Tourette syndrome (TS) is a chronic neurological disorder associated with repetitive, involuntary movements and vocalizations called tics. Many children with TS also experience neurobehavioral problems such as inattention, hyperactivity, and impulsivity—symptoms that overlap with attention deficit hyperactivity disorder (ADHD). In fact, it is estimated that approximately 60 percent of youth with TS also have ADHD. We have recently completed a study suggesting that co-occurring ADHD may be at the root of attention problems in children with TS. The study was published in the November 2010 issue of the *Journal of the American Academy of Child & Adolescent Psychiatry*.

To explore the role of co-occurring ADHD on neuro-

and served as a comparison group. We used well-known, standardized measures to evaluate the children's performance on tasks requiring a variety of cognitive and motor skills. Sustained attention and inhibitory control were evaluated with the Conners' Continuous Performance Test by showing participants various letters on a computer screen and telling them to press a button when they saw certain letters but not press the button when they saw a

non-target letter. To examine cognitive inhibition participants were shown an array of dots on sheets of paper and asked to name their color (red, green, blue) as quickly as possible in the Stroop test. In related tasks, participants were shown pages with similarly arrayed words



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small pegs in a specially designed pegboard in 30-second trials using only their dominant

hand, only their non-dominant hand, and both hands at the same time. The Beery Visual-Motor Integration Test was used to evaluate visual-motor integration with participants copy-

ing 24 geometric designs, presented in order of increasing difficulty.

The results of the study indicated that children with TS+ADHD showed similar problems with sustained attention as children with ADHD only. However, unlike those with ADHD only, children with TS+ADHD performed at the same level as the comparison group on all other tasks. Children with TS only performed at the same level as the comparison group in tasks involving response inhibition and visual-motor integration. They performed at a slightly lower level than comparison children on the fine motor control task. Girls with TS only scored higher than boys with TS only on fine motor control tasks using their dominant hands.

*The study is significant in that it helps to identify brain functions specific to particular disorders and the mechanisms underlying these functions.*

psychological functioning in TS, we studied 236 children, of whom 56 had TS only, 64 had ADHD only, 45 had TS+ADHD, and 71 had neither

“red” printed in green ink) and asked to read the words as quickly as possible. In the Purdue Pegboard Test of fine motor control participants placed

(Continued from page 7)

The study is significant in that it helps to identify brain functions specific to particular disorders and the mechanisms underlying these functions. Similarities in performance between children with TS+ADHD and those with ADHD only suggest that co-occurring ADHD may underlie attention problems in children who have TS. We also observed that the children with TS only didn't show impairment in response inhibition, lending support to a theory that

such children develop compensatory brain mechanisms in an effort to control involuntary tics. Past imaging studies have shown that, during tasks involving response inhibition, children with TS have greater than normal activity in brain areas associated with cognitive control. Differences in fine motor skills between girls and boys with TS may indicate differing developmental pathways and patterns of brain growth between the sexes. Because problems with fine mo-

tor control in childhood are associated with more severe tics in adulthood, our finding of gender difference in motor control of children with TS suggests the need to study whether developmental trajectories of tics may differ in boys and girls. We are now conducting other studies in children and adolescents with TS to help advance the understanding of how neuropsychological functions and their neural correlates are associated with this disorder.

## Real-time Functional Imaging Provides a Novel Form of Biofeedback that May Help TS Patients Control their Symptoms

Michelle Hampson, Ph.D.

Researchers at the Yale Magnetic Resonance Research Center have set up a new system for real-time functional magnetic resonance imaging (fMRI). This system allows us to provide people with information about activity in specific parts of their brain during a functional imaging session. Using this information as a training signal, people can learn to control their brain patterns. This new form of biofeedback has therapeutic potential for a wide array of mental illnesses. We are investigating its potential in the context of Tourette syndrome (TS) and Obsessive Compulsive Disorder (OCD).

### Tourette Syndrome

We believe hyperactiv-

ity in the supplementary motor area (SMA) of the brain may give rise to the urge to tic in patients with TS. This hypothesis is based on a range of evidence. First, as reported by Dr. Itzhak Fried and colleagues in 1991, electrical stimulation of this region produces movements and "urges to move" that resemble the symptoms of TS. Second, many imaging studies have implicated hyperactivity in the SMA in tics, and a recent imaging study by our group (funded by the Tourette Syndrome Association, published in *Biological Psychiatry* in 2009)

highlighted this region as the one area of the brain that was more active during tics than during matched, intentional



Michelle Hampson, Ph.D.  
Research Scientist  
Diagnostic Radiology

movements. Finally, there have been reports of success in treating TS by using repetitive transcranial magnetic stimulation to suppress activity in the region. Thus, we are interested in whether a biofeedback paradigm that trains TS patients to control their SMA activity could yield

clinical benefits.

However, before embarking on a clinical study, we first wished to investigate whether biofeedback could en-



able healthy subjects to control activity in this part of the brain, and to examine how that biofeedback altered their brain dynamics. We recently completed a study of healthy controls addressing these issues (funded by the Dana Foundation, currently in press in *Brain Connectivity*). Eight healthy subjects came in for four sessions of rt-fMRI biofeedback on four separate days. During the biofeedback, they were cued to alternately increase and decrease activity in their SMA, and were provided with a feedback signal indicating their success throughout the scan. In their first session, subjects were unable to exert significant control over this part of the brain. We did not find a significant increase in control across sessions. However, in the later sessions, subjects did exert significant control over activity in their SMA. This suggests that, after some biofeedback training, people can control activity in their supplementary motor area.

We also examined how the biofeedback changed subjects' brain dynamics. We as-

sessed functional connectivity between the SMA and other parts of the brain (functional connectivity is believed to reflect the degree of interaction between brain areas) both before and after the biofeedback.

*...we are interested in whether a biofeedback paradigm that trains TS patients to control their SMA activity could yield clinical benefits.*

We found that functional connectivity between the SMA and subcortical parts of the brain decreased over the course of the biofeedback intervention. This is promising given the large literature implicating subcortical regions in TS. If the intervention has a similar effect on TS patients, it may reduce unhealthy subcortical influences on motor cortical regions, and thereby reduce tic symptoms.

The next step is to run a biofeedback study targeting the SMA in patients with Tourette syndrome to determine whether this intervention can yield clinical benefits.

### Obsessive-Compulsive Disorder

Hyperactivity in a region of the brain called the orbitofrontal cortex has been reported in patients with OCD during symptom provocation tasks, and also in healthy controls during tasks that induce contamination anxiety or anxiety related to the need to check on something important (e.g., whether the stove was left on, whether the door was locked). We are interested in the clinical potential of a biofeedback paradigm that trains OCD patients to control activity in their orbitofrontal cortex.

As a first step, we are investigating whether healthy subjects can learn to control the part of their orbitofrontal cortex involved in contamination-related anxiety, and if so, if this increased control translates into a reduction in anxiety induced by contamination-related images. This is an ongoing study funded by NIH. Depending on the results, we may pursue clinical studies using a similar paradigm in patients with OCD.

For further information regarding these studies, please contact Dr. Michelle Hampson ([michelle.hampson@yale.edu](mailto:michelle.hampson@yale.edu)).

**Please visit our website at [www.yale.tsocd.org](http://www.yale.tsocd.org)  
Find us on Facebook, keyword "Yale Child Study Tourette"**

**Thank you to Virginia Eicher, Lily Katsovich and Nancy Thompson for making the TS/OCD Research newsletter possible!**

## Oxytocin, OCD and Love

Ilanit Gordon, Ph.D.

Studies in animals have repeatedly implicated the hormone oxytocin in social relationships – including offsprings' attachment to caregiver, affiliation, sexual behavior, pair bonding, and parental care. However, oxytocin's exact role in human attachment is much less well understood.

Oxytocin is produced both in the brain and in the body. It is probably the most abundant neuro-hormone in the nervous system and it is named for the “quick delivery” it induces due to its role in uterine contractions during birth. It is very well known for this role as well as for its involvement in breastfeeding and yet continuing discoveries suggest that there may be much more to the oxytocin story.

In a study comparing oxytocin levels, Dr. Leckman and colleagues at the Child Study Center examined levels of oxytocin in the cerebrospinal fluid of adults with OCD and found elevated levels compared to adults with Tourette syndrome and/or healthy participants. How could this finding be related to oxytocin's role in mothering, relationships and social bonding? Thinking about what is unique during moments



Ilanit Gordon, Ph.D.  
Postdoctoral Fellow  
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in which we are bonding to other people (romantic attachments or parental bonding for instance), researchers came up with an intriguing idea: perhaps there is some association between oxytocin and the "obsessive-like" state of mind we all normally get into when we are falling in love with another. Perhaps that could be the connection between OCD, parenthood and romance.

Inspired by this notion, my PhD research aimed to characterize oxytocin levels in new mothers and fathers during the period of transition to parenthood – a time when they are bonding to their new infant and are most mentally and

lowed 160 new mothers and fathers (and their infants) during the 2<sup>nd</sup> and 6<sup>th</sup> postpartum months. I met with mothers, fathers and infants and examined their oxytocin blood levels. Additionally, I assessed how the parents interacted with their infant, videotaping them playing together. First of all, I found that oxytocin levels in the blood were very consistent throughout time; parents' concentrations of oxytocin did not alter significantly from the 2<sup>nd</sup> to the 6<sup>th</sup> month of parenthood. The most surprising finding (considering how oxytocin was thought to be mainly a maternal hormone) was that mothers' and fathers' oxytocin levels in the blood were similar. This was also the case in a different study of adults that were not yet parents

*...perhaps there is some association between oxytocin and the "obsessive-like" state of mind we all normally get into when we are falling in love with another. Perhaps that could be the connection between OCD, parenthood and romance.*

physically preoccupied with their new role as parents and their infant's well-being.

In my research I fol-

lowed 160 new mothers and fathers (and their infants) during the 2<sup>nd</sup> and 6<sup>th</sup> postpartum months. I met with mothers, fathers and infants and examined their oxytocin blood levels. Additionally, I assessed how the parents interacted with their infant, videotaping them playing together. First of all, I found that oxytocin levels in the blood were very consistent throughout time; parents' concentrations of oxytocin did not alter significantly from the 2<sup>nd</sup> to the 6<sup>th</sup> month of parenthood. The most surprising finding (considering how oxytocin was thought to be mainly a maternal hormone) was that mothers' and fathers' oxytocin levels in the blood were similar. This was also the case in a different study of adults that were not yet parents

group, but levels for males and females were similar to each other. Finally, mothers who had higher levels of oxytocin tended to play more with their infant in an affectionate way (singing to them, gazing at their face positively and caressing them) and

fathers with higher levels tended to play positively with their infants with more toys and a lot of changes in position in space.

These results highlight that oxytocin can be measured reliably in the blood as well as in cerebrospinal fluid, and that

its concentration may reflect how positively parents interact with their new infant and how engaged they are with him/her. It is hoped that further exploration of this important hormone may help to illuminate its role in OCD.

## Tourette Syndrome and the Nintendo Wii

Andrew Kobets, M.D. Candidate

Tourette syndrome (TS) was first characterized by Georges Gilles de la Tourette in 1884 after describing 9 people with “maladie des tics.” Tics are brief, repetitive, fragmented movements or sounds, which can cause a great deal of discomfort for patients who have them and which are dynamically molded by the passage of time, the development of the individual and the various social and environmental factors influencing their lives. Patients often report that stress, anxiety, and fatigue worsen tics, while factors such as relaxation, concentration and attention to tasks reduce their severity and frequency.

In Oliver Sacks’ story, “A Surgeon’s Life,” Dr. Sacks describes the story of a surgeon who lived with severe motor and vocal tics which included



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lunging, high pitched squealing, compulsive touching, tapping, ordering, echolalia, darting and gesturing. However, during complex tasks such as driving or operating, his tics quite interestingly disappeared. Dr. Sacks writes “It is only if the operation is broken for a few minutes--to review a special X-ray taken during the surgery--that Bennett, waiting, unoccupied, remembers that he is Tourettic, and in that instant, he becomes so. As soon as the flow of the operation resumes, the Tourette's, the Tourettic identity, vanishes once again.”

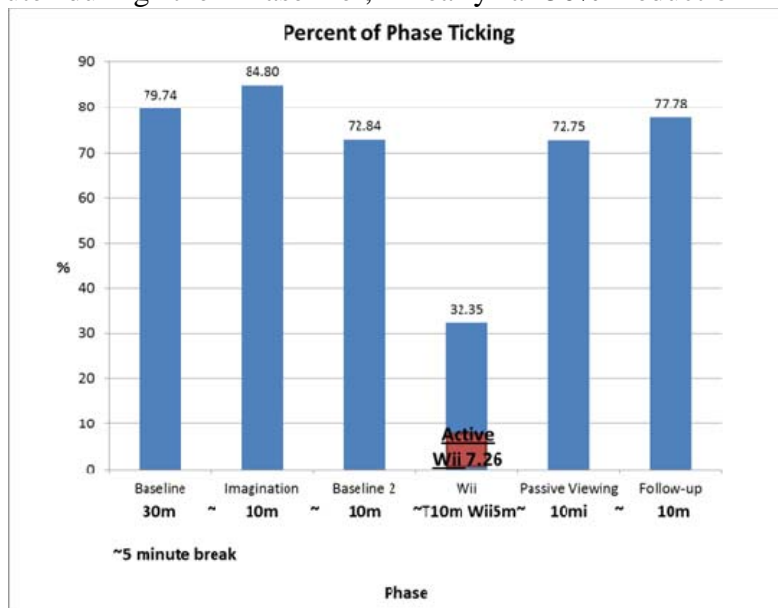
At the Child Study Center, we are currently testing the hypothesis that actively participating in purposeful, engaging and coordinated movement can acutely reduce

tics in kids and adults with TS. We test this hypothesis uniquely using a commercially-available, enjoyable, and well recognized medium: the Nintendo Wii. Tics are surveyed between various “baseline” periods, when a participant is sitting in a room and ticing freely, and also during periods when they are actively playing the Wii tennis practice level 1. The game requires that participants move their bodies as though they were actually returning tennis serves in a continuous series. The graph displays the percentage of time spent ticing during various study segments for a single pa-

*...we are currently testing the hypothesis that actively participating in purposeful, engaging and coordinated movement can acutely reduce tics in kids and adults with TS.*

tient with bouts of severe vocal and motor tics. As documented, this person consistently ticced between 72% and 80% of every minute during the 'Baseline',

phase. Interestingly, however, during the 10 minute period of actively playing Wii, ticcing time fell dramatically to 32%, or nearly a 50% reduction from



'Baseline 2' and 'Follow-up' periods, when he sat with the researcher and was instructed to tic comfortably in front a camera. Although these three periods were separated in time by the other periods of the study, they were highly consistent with each other. The 'passive viewing' period showed similar frequency as the subject sat in the room watching a video of someone playing a game on the Wii. During the 'imagination' period, he was instructed to concentrate on and imagine making movements with different parts of his body. Tics rose slightly to 51 seconds out of every minute, or 84.8% of the time for this

baseline. When we looked closer at specifically the 5 minutes when he was fully engaged in the game and not passively waiting between successive rounds, he only ticced for 22 seconds total, or 7.26% of the five minute segment.

While this subject almost immediately returned to his baseline frequency of ticcing afterwards, our findings provide several interesting observations. First, there appeared to be a substantial reduction in tics while this individual was actively engaged in coordinated movement and concentration. Secondly, there appeared to be no "rebound effect" in periods after

the Wii gameplay, suggesting that acutely reducing tics does not result in a compensatory period afterwards when they increase in frequency. Thirdly, thinking about one's own movements, as in the imagination period for this patient, may in some way exacerbate an individual's tics. In fact, not paying attention to tics during active engagement in the Wii game may have additionally contributed to their reduction.

While it was interesting to see tics nearly "disappear" during gameplay, it is unknown whether these effects provided any control over thoughts and movements, whether they reduced awareness of their urgency, or whether they can have any long-term influence in managing symptoms. In addition, it also begs one to consider whether the effect can be replicated in any other personally engaging activities (playing a musical instrument, dancing, playing sports) by eliciting a similar focus that "teaches" a person suffering with TS to better manage symptoms. These are the types of questions we hope to investigate with the new generation of work being performed at the Yale Child Study Center. For more information or questions about this study, please contact Andrew Kobets ([Andrew.Kobets@Yale.edu](mailto:Andrew.Kobets@Yale.edu)).

**Please visit our website at [www.yale.tsocd.org](http://www.yale.tsocd.org)  
Find us on Facebook, keyword "Yale Child Study Tourette"**



# Does Tourette Syndrome Have a Link to Creativity?

Carlotta Zanaboni, Ph.D.

Well, the answer seems to be yes! At least if you consider Mozart, Molière and Johnson as artists! It's possible they actually had Tourette syndrome (TS).

## Anatomic and Functional Bases

Tourette syndrome has a neurophysiologic origin in at least five following interdependent frontal cortico-subcortical circuits: dorsolateral prefrontal circuit, lateral orbitofrontal circuit, anterior cingulate circuit, oculomotor circuit, and motor circuit. They program and structure movements and are involved in the reception, interpretation and elaboration of sensory input and in the elaboration of motor output, too.

Surprisingly, creativity and divergent thinking also activate the dorsolateral prefrontal circuit and anterior cingulate circuit of the frontal cortex. In particular, the frontal lobe is linked with idea generation; this phenomenon is clearest in verbal creativity, but it also shapes non-linguistic creativity.

## Tourette Syndrome: One Core, Two Personality Sides

The assumption that TS is linked to creativity is memorably described by a professor of Clinical Neurology at the Al-

bert Einstein College of Medicine in New York, Oliver Sacks (1992). Following is his distinc-



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tion between the stereotypic form and the phantasmagoric form of TS: *"At one extreme is the stereotypic form with its simple motor tics, iterations, perseverations, and brief, explosive vocalisations. At the other extreme is an elaborate, innovative, phantasmagoric form which is especially remarkable for its mimicry, antics, playfulness, extravagance, impudence, audacity, inventions, dramatisations, unexpected and sometimes surreal associations, intense and uninhibited affects, speed, "go," vivid imagery and memory, hunger for stimuli and incontinent reactivity, and constant reaching into inner and outer worlds for new material to Tourettise, to permute and transform."* He also emphasizes

the possibility of patients leveraging TS into an orderly flow, producing artistry with extraordinarily creative features. For instance, this is how a famous jazz musician found a way to treasure his disease and discovered the inseparability between his TS and creativity. *"Rhythm and Tourette Syndrome have been intertwined from the first day I found that drumming on a table could mask my jerky hand, leg and neck movements... could harness my unbounding [Tourettic] energy, directing it into an orderly flow"* (Aldridge, 1980). According to mathematician Henri Poincaré, creativity is *"the union of pre-existing elements that produce new and useful combinations."*

## Research in Italy

Starting with the hypothesis that those with TS are more creative than those without, I conducted a study in Italy (Porta & Zanaboni, 2010) at IRCSS Galeazzi of Milan involving 23 TS children/adolescents (6-18 years old), their teachers, and parents, and a control group using Williams' Divergent Thinking Test, Creative Personality Test and Williams Rating Scale.

Williams' model states that the main features of creativity are thinking-cognitive-divergent factors (fluidity, flexi-

(Continued on page 14)



bility, originality, elaboration) and personality-emotional-divergent factors (curiosity, imagination, complexity, risk taking).

Results from the flexibility subtest of the Divergent Thinking Test confirm our initial hypothesis that creativity would be statistically higher in the TS group than in the control sample. Flexibility is the ability to change your approach towards a stimulus, the capability to pass from one category to another, and change your mind set to avoid obstacles.

#### **Research in the U.S.**

I repeated the study with a sample of 18 Tourette patients at the Yale Child Study Center, and the main results confirm that flexibility is more likely to be developed in Tourette patients than in the control group. Additionally, the findings of this second study found fluidity to be more developed in the clinical sample than in controls. Fluidity is the ability to quickly consider a huge quantity of ideas and then generate a large number of valid responses.

#### **Medication Treatments: the Role of Dopamine**

Tourette syndrome presents an altered dopaminergic synaptogenesis, which sometimes has to be managed with medications in addition to psychological support. At the same time, creative personality is influenced by mesolimbic dopamine, especially when measured by Novelty Seeking and Crea-

tive Drive categories.

While medications used to treat TS and creativity are both linked to the same dopaminergic, serotonergic and noradrenergic systems, medication can only produce an intensification of preexisting personality traits and artistic skills and does not cause a genuine improvement in artistic-creative skills. Thus it is possible to assume that creative-divergent skills truly belong to patients and they are not merely a psychotropic effect.

relationship styles to soften OC symptoms. Potentially it could also improve these patients' social skills and self-efficacy, bolstered by public approval from the final performance. This could cause a shift away from the immediate satisfaction given by the impulsive pleasure of tic manifestation towards a more gradual and controlled one given by the creative product and by extension of cognitive-behavioral patterns learned outside the therapeutic context.

The school environment

*As a treatment supplement to medications and/or other psychological techniques such as Habit Reversal Training, Tourette patients may benefit from therapeutic programs including visual arts, music, acting and dance.*

#### **Interventions Based on Creativity**

As a treatment supplement to medications and/or other psychological techniques such as Habit Reversal Training, Tourette patients may benefit from therapeutic programs including visual arts, music, acting and dance. For instance, therapeutic acting or role play could incorporate body activity to deal with ADHD and the practice of new cognitive-behavioral and interactive-

is often difficult for TS patients. Ideally, by introducing psycho-educational classes for teachers, parents and students and a recreational lab for classmates of Tourette students, an otherwise stressful context could become a supportive or even therapeutic setting. All too often, TS students are ignored, misunderstood and discriminated against in school, instead of having their classmates and teachers learn and use appropriate conduct with them. A TS creative

school lab could first take into account motor and linguistic limitations in choosing themes and activities, then include simple tasks to avoid feelings of failure on the part of the patients, as well as exclude tasks that may highlight symptomatology to prevent embarrassment or tiredness.

### Conclusion

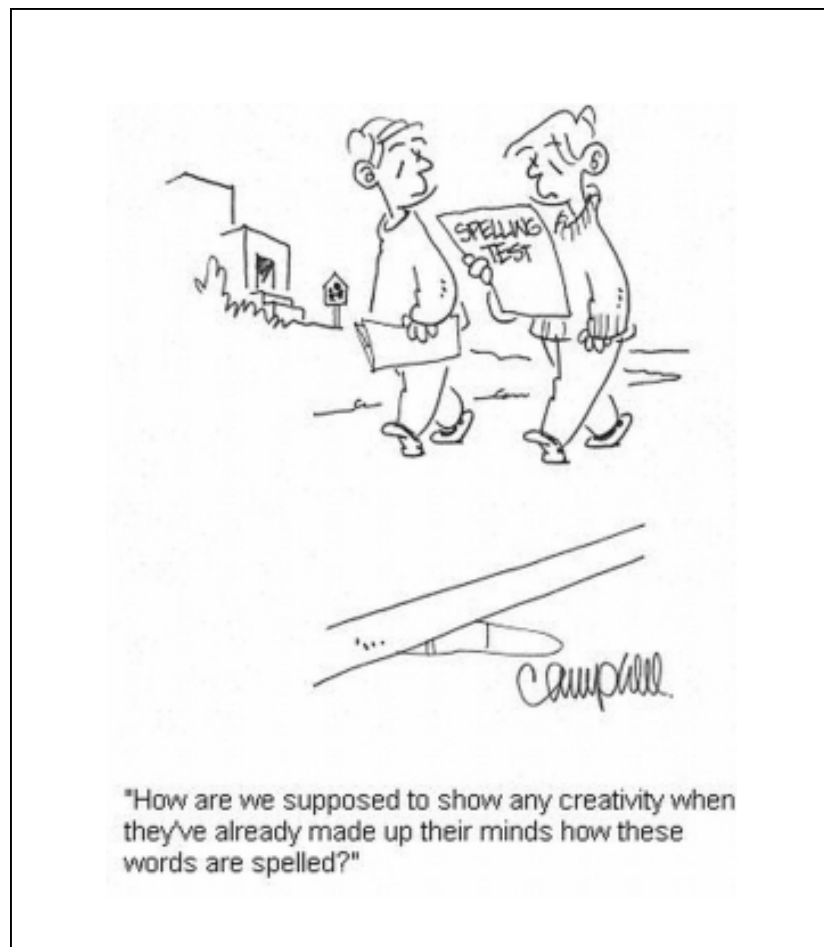
The general correlation between psychopathology and creativity has already been ex-

plored in evolution theories (Huxley, 1964). According to Huxley, because psychopathology has a genetic component, it must show some positive aspects; creativity is one of them. According to Csikzentmihaly (1998), creativity is one's ability to use cognitive and aesthetic skills and empathy towards cultural evolution.

The link between TS and creativity has been verified empirically. Many TS patients have a strong expressive-

creative predisposition that treatment providers and caregivers may use to maximize therapeutic benefit.

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