The Big Picture
“Sometimes when I was slicing food, in the kitchen at home, I would get these ideas about cutting up my parents...”
It was clear that Alex did not wish to harm anyone—he was simply unable to screen out thoughts of doing so.
**NRS:** Other problems or thoughts that might lead you to be concerned that you hurt someone?

**Patient:** Um, the only violent image I’ve had is of my mother and when I hug her, her head would fall off. A very graphic image… And then I would have a ritual of a different way of approaching her… a different way of embracing her that would keep that from happening.

**NRS:** You’d hug her and then your got this image and that would make you feel very anxious.

**Patient:** Yeah

**NRS:** And you wouldn’t want to hurt your mother?

**Patient:** No, No!
Like a sneeze that keeps building or an itch that won’t go away... the tag on the back of your shirt collar...
Some disorders characterized by deficient inhibition (gating) of motor, cognitive or sensory information:

- Obsessive Compulsive Disorder
- Tourette Syndrome
- Schizophrenia
- Huntington’s Disease
How the brain works

MOTOR ACTIVITY

POSTURE

MOVEMENT

GATE CONTROL:
IN VolUNTARY (eg. VESTIBULAR)
VOLUNTARY (eg. APPETITIVE)

COGNITIVE, SENSORY
AND EMOTIONAL ACTIVITY

CONSCIOUSNESS

GATE CONTROL:
PRECONSCIOUS (eg. ATTENTION)
CONSCIOUS (eg. CONCENTRATION)

DETERMINANTS OF GATING CAPACITY:

GENETIC
DEVELOPMENTAL
ENVIRONMENTAL
PATHOLOGICAL
The anatomy of the direct pathways of the frontal-subcortical circuits

Prefrontal Cortex
  ↓
  Caudate (Dorsolateral)
  ↓
  Globus pallidus (Lateral dorsomedial)
  ↓
  Thalamus (VA and MD)

Lateral Orbital Cortex
  ↓
  Caudate (Ventromedial)
  ↓
  Globus pallidus (Medial dorsomedial)
  ↓
  Thalamus (VA and MD)

Anterior Cingulate Cortex
  ↓
  Nucleus Accumbens
  ↓
  Globus pallidus (Rostrolateral)
  ↓
  Thalamus (MD)
C -----> S -----> P -----> T
Spiny I GABAergic neuron
Resting FDG-PET in OCD
O-15 PET and Symptom Provocation in OCD
“OK, Captain Anxiety. I took some Polaroids before we left. Exhibit A: the stove with all burners clearly in the “off” position. Exhibit B: the back door with its deadbolt latched. Exhibit C: my curling iron unplugged.”
fMR BOLD during implicit learning

OCD Group

Normal Control Group
Obsession ⇒ Anxiety ⇒ Compulsion

Repetitive
Undesired/Unwilled
“Compelled”
# Clinical Summary: OCD and TS

<table>
<thead>
<tr>
<th></th>
<th>OCD</th>
<th>TS</th>
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<tbody>
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<td>Prevalence</td>
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<td>MZ Concordance</td>
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<td>75-90+%</td>
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<tr>
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<td></td>
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<tr>
<td>Associated conditions</td>
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<td>ADHD, Rage, SIB</td>
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<td></td>
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<td></td>
<td>CBT</td>
<td>Habit Reversal</td>
</tr>
</tbody>
</table>
## DSM-IV OCD Field Trial

### Content of Primary Obsessions (N = 425)

<table>
<thead>
<tr>
<th>Obsession</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contamination</td>
<td>37.8%</td>
</tr>
<tr>
<td>Fear of Harm</td>
<td>23.6%</td>
</tr>
<tr>
<td>Symmetry</td>
<td>10.0%</td>
</tr>
<tr>
<td>Somatic</td>
<td>7.2%</td>
</tr>
<tr>
<td>Religious</td>
<td>5.9%</td>
</tr>
<tr>
<td>Sexual</td>
<td>5.5%</td>
</tr>
<tr>
<td>Hoarding</td>
<td>4.8%</td>
</tr>
<tr>
<td>Unacceptable Urges</td>
<td>4.3%</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>1.0%</td>
</tr>
</tbody>
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### DSM-IV OCD Field Trial

Content of Primary Compulsions (N = 425)

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<thead>
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<th>Compulsion</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checking</td>
<td>28.2%</td>
</tr>
<tr>
<td>Cleaning/washing</td>
<td>26.8</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>11.8</td>
</tr>
<tr>
<td>Repeating</td>
<td>11.1</td>
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<tr>
<td>Mental Rituals</td>
<td>10.9</td>
</tr>
<tr>
<td>Ordering</td>
<td>5.7</td>
</tr>
<tr>
<td>Hoarding/collecting</td>
<td>3.5</td>
</tr>
<tr>
<td>Counting</td>
<td>2.1</td>
</tr>
</tbody>
</table>
Quality of Life with OCD

Relationships
- 92% lowered self-esteem
- 73% interfered with family relationships
- 62% fewer friends or difficulty in maintaining friendships

Education
- 58% lowered academic achievements

Work
- 66% lowered career aspirations
- 47% interfered with work
- 40% unable to work; average loss of 2 years

Suicide Attempts
- 13% suicide attempts secondary to OCD symptoms
LASSIE!
GET HELP!!
Effectiveness of Fluoxetine in OCD

Fluoxetine (mg/day)
PBO  20  40  60

Δ YBOCS

Fluoxetine (mg/day)
PBO  20  40  60

Δ YBOCS
The rate of glucose metabolism in the right caudate nucleus decreased more in OCD patients who responded to cognitive-behavioral therapy than in patients who did not respond.
Professor Lundquist, in a seminar on compulsive thinkers, illustrates his brain-stapling technique.
Electrical deep brain stimulation in OCD:

Nucleus accumbens / Anterior limb of the internal capsule

Reduced OFC/ACC metabolism shown by FDG-PET

Greenberg et al. 2006
FIGURE 1. Percent Expression of D8/17 Antigen on B Lymphocytes in 31 Patients With Childhood-Onset Obsessive-Compulsive Disorder and/or Tourette’s Syndrome and in 21 Healthy Comparison Subjects

\(^{a}\)Horizontal line through scatter plot represents the group mean.
The diagnostic criteria for PANDAS (Swedo et al, 1997) are:

1. The diagnosis of OCD and/or a tic disorder
2. Symptom onset between ages 3 years and puberty;
3. Episodic course of illness characterized by an abrupt onset of symptoms or frequent, dramatic exacerbations;
4. Symptom exacerbations are associated with GABHS infection;
5. Presence of neurological abnormalities such as motor hyperactivity or adventitious movements, including choreiform movements (not chorea) or tics.
Tourette’s Syndrome

Premonitory Urge $\Rightarrow$ Discomfort $\Rightarrow$ Tic

Repetitive
Undesired/unwilled
“Compelled”
“Definite TS” (or Tourette’s Disorder)*

(tic: sudden, rapid, recurrent, non-rhythmic, stereotyped movement or vocalization)

A. Multiple motor and ≥ 1 vocal tic at some time
B. Tics occur many times per day, nearly every day, or intermittently for 1 year (with no tic-free period > 3 months)
Tics change over time
C. Onset < 21 (18)
D. Exclusion Criteria
Witnessed live or taped by a reliable examiner

*TSA Classification Study Group vs. (DSM-IV)
Like a sneeze that keeps building or an itch that won’t go away… the tag on the back of your shirt collar…
"Three times a week, lecturing on cell biology to 400 university students, I forge through an intensely focused hour in the spotlight without a single tic. But throughout the lecture my premonitory sensations build up steadily, urgently, like God's own sneeze. So I must follow this period of submergence by climbing the stairs to the privacy of my office, a dolphin coming up to breathe, there to tic, tic, tic... until the need subsides. Like a terrible itch you can ignore, for a little while, Tourette tics call into question our glib definitions of voluntary and involuntary behavior."

P. Hollenbeck, Ph.D. Cerebrum 2003
## Clinical Summary: OCD and TS

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Reduced basal ganglia volumes in Tourette’s syndrome using three-dimensional reconstruction techniques from magnetic resonance images

B. Peterson, MD; M.A. Riddle, MD; D.J. Cohen, MD; L.D. Katz, MD; J.C. Smith, BA; M.T. Hardin, MSN; and J.F. Leckman, MD

Article abstract—Using a 1.5-tesla GE Signa MR scanner, we imaged the brains of 14 right-handed Tourette’s syndrome (TS) patients (11 men, three women), aged 18 to 49 years, who had minimal lifetime neuroleptic exposure. We also studied an equal number of normal controls individually matched for age, sex, and handedness and group-matched for socioeconomic status. We circumscribed basal ganglia on sequential axial images from spin-echo proton density-weighted acquisitions (TR 1,700, TE 20; slice thickness, 3 mm with 1.5-mm skip) and submitted the images for three-dimensional processing at a computer graphics workstation. Our hypothesis of lenticular nucleus volume reduction in TS was confirmed for the left- but not the right-sided nucleus. Post hoc analyses revealed smaller mean volumes of the caudate, lenticular, and globus pallidus nuclei compared with controls on both the right and left. Further analyses of basal ganglia asymmetry indices suggest that TS basal ganglia do not have the volumetric asymmetry (left greater than right) seen in normal controls. These findings confirm and extend prior phenomenologic, neuropathologic, and neuroradiologic studies that implicate the basal ganglia in the pathogenesis of TS.

NEUROLOGY 1993;43:941-949
Bloch et al., 2005
NAcc volume: TS versus normal controls (23 TS, 23 NC)

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<th>TS Subjects</th>
<th>Control Subjects</th>
<th>Significance</th>
</tr>
</thead>
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<tr>
<td>Right NAcc GM Density</td>
<td>0.53 ± 0.11</td>
<td>0.66 ± 0.06</td>
<td>0.000035</td>
</tr>
<tr>
<td>Left NAcc GM Density</td>
<td>0.56 ± 0.10</td>
<td>0.67 ± 0.06</td>
<td>0.000041</td>
</tr>
<tr>
<td>Right NAcc Volume (mm³)</td>
<td>347 ± 63</td>
<td>409 ± 58</td>
<td>0.00112</td>
</tr>
<tr>
<td>Left NAcc Volume (mm³)</td>
<td>385 ± 50</td>
<td>445 ± 69</td>
<td>0.00174</td>
</tr>
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Comparable age and gender distributions. Unpaired Student’s t-tests
Increased ventral striatal monoaminergic innervation in TS

Albin et al. 2003
Antibodies against human putamen in children with Tourette syndrome

H.S. Singer, MD; J.D. Giuliano, MSN; B.H. Hansen, BS; J.J. Hallett, MD; J.P. Laurino, PhD; M. Benson, BA; and L.S. Kiessling, MD

Article abstract—Background: Similar to the model for Sydenham’s chorea, antineuronal antibodies, which develop in response to a preceding streptococcal infection, have been speculated to have a role in the development of Tourette syndrome (TS). Methods: Serum antibodies against human caudate, putamen, and globus pallidus (interna and externa) were assayed by enzyme-linked immunosorbent assay (ELISA) and Western blot techniques and results were correlated with clinical characteristics and markers of streptococcal infection. Subjects: A total of 41 children with TS (mean age, 11.3 years) and 39 controls (mean age, 12.1 years) were included. Results: Compared with controls, TS subjects had a significant increase in the mean (p = 0.006) and median (p = 0.002) ELISA optical density (OD) levels of serum antibodies against putamen, but not caudate or globus pallidus. Western blots on 20 control and 20 TS serum samples showed that specific antibodies to caudate/putamen occurred more frequently in TS subjects at 83, 67, and 60 kDa; antigens were present in a synaptosomal fraction. TS subjects with a positive family history of tics had higher OD values (p ≤ 0.04), but no association was shown with age of tic onset, tic severity, sudden onset of tics, or presence of attention-deficit hyperactivity disorder or obsessive-compulsive disorder. Risk ratio calculations in TS and control groups and in study subjects dichotomized for high and low putamen OD values were similar for titers of antistreptolysin O ≥ 166 or antideoxyribonuclease B ≥ 170. A subgroup analysis limited to subjects with elevated streptococcal titers, however, showed a significantly (p ≤ 0.004) larger number of TS subjects with elevated OD levels. Conclusion: Children and adolescents with TS had significantly higher serum levels of antineuronal antibodies against putamen than did controls, but their relation to clinical characteristics and markers for streptococcal infection remains equivocal.
TS pedigrees reveal strong heritability of TS phenotypes
Leckman et al. Familial developmental pattern of tic severity
Efficacy of Habit Reversal Therapy (HRT) in Adults with TS

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment (N)</th>
<th>Yale Global Tic Severity Scale (YGTSS) – Total Tic Score</th>
<th>Effect size (d)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-treatment (SD)</td>
<td>Post-treatment (SD)</td>
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<tr>
<td>Wilhelm et al., 2003</td>
<td>HRT (16)</td>
<td>30.5 (7.1)</td>
<td>19.8 (7.6)</td>
</tr>
<tr>
<td></td>
<td>SP (13)</td>
<td>26.6 (7.8)</td>
<td>26.9 (9.2)</td>
</tr>
<tr>
<td>Deckersbach et al., in press</td>
<td>HRT (15)</td>
<td>29.3 (5.8)</td>
<td>18.3 (5.2)</td>
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THE SPECTRUM CONCEPT

Who in the rainbow can draw the line where the violet tint ends and the orange tint begins? Distinctly we see the difference of the color, but where exactly does the first one visibly enter into the other? So with sanity and insanity.

Herman Melville
Billy Budd
COMPULSIVITY AND IMPULSIVITY

DIFFERENCES AND SIMILARITIES IN SYMPTOMS

DIFFERENCES

• DRIVING MECHANISM IN COMPULSIVITY IS REDUCTION OF DISCOMFORT

• DRIVING MECHANISM IN IMPULSIVITY IS OBTAINING AROUSAL OR SATISFACTION

SIMILARITIES

• INABILITY TO DELAY REPETITIVE BEHAVIORS
Impulse Control Disorders (ICD)

DSM-IV

Substance/related disorders
Paraphilia
[Intermittent Explosive Disorder]
Kleptomania
Pyromania
Pathological Gambling
[Trichotillomania]
ICD/not otherwise specified

Non DSM IV ICDs
Compulsive Shopping
[Repetitive self mutilation/self injurious behavior]
My hair pulling terrified me. The results were devastating, and yet, when I entered a pulling trance, which would often last for hours, it was as if I was doing exactly what was necessary.
The Self-Injurious Continuum

**Lower lethality**
- Onychophagia
- Skin cutting

**Higher lethality/psychosis**
- Cigarette burning
- Autoenucleation
- Autocastration
- Autosurgery

**Trichotillomania**
- Lip/finger chewing
- Head banging
The Big Picture