"THEY TRIED TO MAKE ME GO TO REHAB"

Mary ET Boyle, Ph. D.
Department of Cognitive Science
UCSD
A Tribute to Amy Winehouse

Updated July 20, 2012, 5:42 a.m. ET

One wet and windy December evening in 2006, a 23-year-old Amy Winehouse arrived in Dingle, a fishing town of 2,000 souls in County Kerry, southwest Ireland, “at the edge of the known world before we found out that it was round,” as one resident describes it. There, in front of some 70 people gathered in the small St. James Church, Winehouse performed songs that have forever inscribed her in the musical imagination—“Back to Black,” “ Tears Dry On Their Own,” “You Know I’m No Good.”

Singer Amy Winehouse performs in Dingle

With her second album “Back to Black” not even two months old, the English singer was in Dingle to record “Other Voices,” an Irish TV show that every winter brings musicians from all over the world to this remote corner of Europe. This month, a year after her premature death at 27 from alcohol poisoning, those few hours she spent in the town have been turned into a touching tribute to the tormented artist.

“Arena: Amy Winehouse—The Day She Came to Dingle,” by Irish director Maurice Linnane, brings together unseen footage from Winehouse’s heart-wrenching performance, archival recordings of her musical icons and the recollections of locals who met her that evening.

“We decided we would just tell a story of that day, of what happened when Amy came to Dingle,” says Mr. Linnane, whose film stays away from the rumors and controversies that surrounded the soul artist’s last years. “My rule was, if they weren’t in the room that day, they weren’t allowed to talk about it.”

So we hear about Winehouse from Paddy Kennedy, the Dingle bus driver who picked the singer up at the airport and thought she was Amy Winehouse’s daughter. “I wasn’t sure who the lady was,” he recalls in the documentary. Mr. Linnane adds that she sang in the back of the bus, “half the way from Dingle to Cork.”

We hear from Aiste Woodcock, a music producer on “Other Voices,” whom Winehouse asked to hold her hair while she backcombed it for her signature beehive style. “She came with her spindly, little legs and her mental hair, and sung her heart out, in Kerry, for us,” Ms. Woodcock says.
“As for Ms. Winehouse, her talent was as fierce as her heartache.”

– Sally Satel
The rat in question was placed in a large rectangular box with corners labeled A, B, C, and D and was allowed to explore freely. Whenever the rat went to corner A, Olds pressed a button that delivered a brief, mild electrical shock through the implanted electrodes. (Unlike the rest of the body, brain tissue does not have the receptors that allow for pain detection, so such shocks don’t produce a painful sensation within the skull.) After a few jolts, the rat kept returning to corner A and finally fell asleep in a different location. The next day, however, the rat seemed even more interested in corner A than the others. Olds and Milner were excited: They believed that they had found a brain region that, when stimulated, provoked general curiosity. However, further experiments on this same rat soon proved that not to be the case. By this time, the rat had acquired a habit of returning often to corner A to be stimulated. The researchers then tried to coax the rat away from corner A by administering a shock every time the rat made a step in the direction of corner B. This worked all too well—within five minutes, the rat relocated to corner B. Further investigation revealed that this rat could be directed to any location within the box with well-timed brain shocks—brief ones to guide the rat to the target location and then more sustained ones once it arrived there.
The next day...
Ingestion

- Preferred for many drugs
- Easy and safe
- Carried via bloodstream
- Unpredictable dosage

Injection

- Preferred by medical professionals
- Predictable: fast; strong drugs
- Drug users: IV injection
- Dangerous – allergic rxn or overdose.
**inhalation**

- Through the lungs into the capillaries
- Anesthetics; tobacco & marijuana
- Difficult to regulate dose
- Can damage lungs

**absorption**

- Mucous membranes
- Nose; mouth
- Snort cocaine
NICOTINE’S PATH TO THE BRAIN

Most cigarettes also contain ammonium hydroxide, To maintain neutral pH

From H. Lester, CalTech
Blood nicotine concentrations during and after a cigarette
CLASSIFICATION OF DRUG ACTIONS

- **stimulants**
  - Enhance and speed up CNS activity
  - Temporary effect \(\rightarrow\) crash

- **depressants**
  - Slow down or impair CNS activity

- **Hallucinogens**
  - Distort sensory information processing
Drug Addiction, Dysregulation of Reward, and Allostasis

George F. Koob, Ph.D., and Michel Le Moal, M.D., Ph.D.

“Drug addiction is a chronically relapsing disorder that is defined by two major characteristics: a compulsion to take the drug with a narrowing of the behavioral repertoire toward excessive drug intake, and a loss of control in limiting intake (American Psychiatric Association 1994; World Health Organization 1992).

An important challenge for neurobiological research is to understand the neuroadaptive differences between controlled drug use and loss of control, and by extension, the molecular, cellular and system processes that lead to addiction (Koob and Le Moal, 1997).”

Neuropsychopharmacology (2001) 24, 97–129
The spiraling distress/addiction cycle

- **Preoccupation/anticipation**
- **Positive Reinforcement**
  - Wanting drug
  - Persistent psychological problem
- **Binge/intoxication**
  - Taken in larger amounts than needed
- **Withdrawal/negative affect**
  - Persistent desire
  - Tolerance/withdrawal
- **Spiraling distress**
  - Social, occupational, recreational activities compromised

Adapted from Koob & Le Moal (2001) *Neuropsychopharmacology* 24, 97–129
Drug Effects Over Time

- Administration Phase
- Active Phase
- Metabolism Phase

Drug Effects

Time

active drug  metabolism  inactive drug
DOSE RESPONSE CURVE...

Magnitude of Drug Effect vs. Dose of Drug

Initial dose-response curve
DOSE RESPONSE CURVE...
TOLERANCE & WITHDRAWAL
REWARD SYSTEM DYSREGULATION

Drug effect decreases with increased exposure.

Withdraw from drug.
With no drug to counteract them, the neural adaptations produce withdrawal effects opposite to the effects of the drug.

Drug exposure leads to the development of adaptive neural changes that produce tolerance by counteracting the drug effect.

The magnitude of the withdrawal effect is proportional to the tolerance of the drug.
ALTERING THE FUNCTION OF NEUROTRANSMITTERS CAN CHANGE BEHAVIOR.

**Agonist**
- **mimics** or **facilitates** the release
- More dopamine released

**Antagonist**
- **oppose** or **blocks** the release
- Less dopamine released
MESOTelecephalic DA System

- Nigrostriatal pathway
- Mesocorticolimbic pathway
PLEASURE CENTERS OF THE BRAIN...

ICSS: intracranial self-stimulation
INCREASE IN DA RELEASE IN N. ACCUMBENS...

- **Dopamine Level in Nucleus Accumbens** (percent of baseline)

- **Minutes**

- **Periods of intracranial self-stimulation**

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Dopamine Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>60</td>
<td>200</td>
</tr>
<tr>
<td>90</td>
<td>300</td>
</tr>
<tr>
<td>120</td>
<td>400</td>
</tr>
</tbody>
</table>
Is there a common molecular pathway for addiction?

Eric J Nestler
Drugs of abuse

- Diverse chemicals
- Distinct targets & effects

Cause common effects:

- acute
- chronic

Characterized by:

- Loss of control over drug use.
  - Negative emotional symptoms withdrawal.

- immediate reward → repeated use → addiction
MESOTelecephalic DA system

- Nigrostriatal pathway
- Mesocorticolimbic pathway
All drugs of abuse affect **the limbic system**.

Mesocorticolimbic system → dopaminergic neurons in the ventral tegmental area → NAc.

**Common actions on brain reward circuits**
Examples of common effects on the VTA-NAc.

- **Stimulants** directly *increase* dopaminergic transmission in the NAc.

- **Opiates** do the same (indirectly) they inhibit GABAergic interneurons in the VTA, which *disinhibits* VTA dopamine neurons.

- **Opiates** also *directly* act on opioid receptors on NAc neurons.