M & MDMA:

An active exploration of the biological action of ecstasy.

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ABSTRACT

Using active demonstrations, we helped students understand how the drug of abuse, MDMA ("ecstasy"), interferes with communication in the nervous system. With help from Slide Teaching Packets downloaded at the National Institute on Drug Abuse website, you too can break out a bag of M&Ms and awaken your class to "the agony of ecstasy" (Burgess et al. 2000).

INTRODUCTION

Do your students think that "ecstasy" provides a safe high? They may hear about this drug through media coverage of "rave" night club events where it is popular but hazardous. The chemical name of "ecstasy" is 3,4-methylenedioxymethamphetamine (abbreviated MDMA), and we set forth to dispel the notion that MDMA is a safe party drug. Our active role-play uses M&M chocolate candies to enhance understanding that MDMA interferes with communication in the nervous system. This activity can be used to fulfill national science education standards.

Grade Level

9th Grade or above

Time Requirements

1 block period of 90 min, or 2 class periods of 50 min each

Prerequisites

- Understand the basic structure and function of a cell and its major organelles.
- Know that the neuron is the cellular unit within the brain.
- Be familiar with the unique structure and function of the neuron.
- Understand that drugs are chemicals that can be distributed in the circulatory system.

Student Learning Objectives

- Describe how the nerve terminal, presynaptic membrane, synaptic cleft, and postsynaptic membrane participate in neural communication.
- Understand the basic steps of neurotransmission.
- Understand health-related consequences of MDMA use.
- Identify the biological effects of MDMA to increase release of serotonin.

Correlation with Standards

- National Teacher Standards Correlations
    1. Science in Personal and Social Perspectives (F): Personal and Community Health
    2. Science in Personal and Social Perspectives (F): Science and Technology in Local, National, and Global Challenges
- American Association for the Advancement of Science Benchmarks for Scientific Literacy
- Human Organism: Basic Functions and Human Identity Benchmarks (AAAS 1993)
- NSTA's Scope Sequence and Coordination emphasis on the human organism (NSTA 1993)

SLIDE PACKETS MAKE TEACHER CONTENT PREPARATION EASY.

Introduce the MDMA activity using Powerpoint slides and teaching scripts from the National Institute on Drug Abuse web site (http://www.drugabuse.gov/pubs/Teaching/). Use all or part of the slide show entitled "The Brain and the Actions of Cocaine, Opiates, and Marijuana" to review the brain, neurons, neural communication, and drug effects. Use another slide show entitled "The Neurobiology of Ecstasy (MDMA)" to describe MDMA use specifically. For more information, consult *Brain Facts* or *Neuroscience* (see References).

A BACKGROUND SUMMARY FOR TEACHERS.

The Agony of Ecstasy

"Ecstasy" is 3,4-methylenedioxymethamphetamine, and is also known as MDMA, XTC, X, Adam, Clarity, or Lover's Speed. MDMA is a synthetic chemical similar in structure to methamphetamine (Fig. 1). Usually taken in pill or capsule form, its psychological effects last approximately 3-6 hours and include euphoria, alertness, heightened sense of touch, and empathy for other individuals (Burgess et al. 2000, Gudelsky & Yamamoto 2003). Immediate negative responses can also occur, such as headaches, jaw clenching, blurred vision, nausea, and mental problems (impaired judgment, confusion, anxiety, or sleep disruption). MDMA can also increase heart rate and blood pressure. Dilated pupils sometimes indicate drug use. Several days after these initial effects, users report feeling sad, unsociable, and irritated.

Even a single dose of MDMA can have life-threatening effects. In 2001, approximately 5500 emergency room visits involved MDMA-related cases of dangerously high body temperature, dehydration, hypertension, heart attack, stroke, muscle breakdown, kidney failure, seizures, and cerebral hemorrhage. (See SAMHSA website for more statistics.) Overheated and overcrowded conditions (as found in "raves") exacerbate these problems.

Long-lasting, perhaps permanent, damage to nerve terminals and axons occurs after MDMA use. The drug causes degradation of nerve terminals and axons that secrete the neurotransmitter called serotonin (Gudelsky & Yamamoto 2003, Burgess et al. 2000). Evidence of such damage is observable in the brains of human MDMA users, via the brain imaging technique known as Positron Emission Tomography (PET, McCann et al. 1998, Fig. 2). Low

levels of serotonin are involved in many disorders, including depression, anxiety, impulsivity, and sleep abnormalities.

How does MDMA alter neural communication?

Both short- and long-term effects of MDMA relate to its ability to increase the amount of neurotransmitter in the synapse. Due to similarities in chemical structure (Fig. 1), MDMA replaces several neurotransmitters (serotonin, dopamine, and norepinephrine) at reuptake sites where the neurotransmitters would normally be recycled back into the axon terminal. This causes the neurotransmitters themselves to remain in the synapse longer than usual and continue binding with postsynaptic receptor proteins. What's more, MDMA itself can be transported into the axon terminal where it causes even more neurotransmitter release. (See Fig. 3.)

Finally, MDMA causes degeneration of serotonin axons. By releasing so much serotonin, MDMA weakens the axon terminal. MDMA also causes "superoxidation" (in a way "rusting" the serotonin axon), and excess calcium release inside neurons. Together these processes cause serotonin axons to die off. Without axons, serotonin neurons cannot communicate with other neurons, and thereby may contribute to the long-term detrimental effects of MDMA on behavior, cognition, and mood. Overall, it is clear that MDMA is not safe and can damage the nervous system. The following demo will solidify this message for your students!

GET ACTIVE WITH THE M & MDMA DEMO

Materials

3 plastic bowls
1 plastic funnel (big enough for M&Ms to pass through)
4 small jars with lids (baby food jars)
~100 green M&Ms
~100 blue M&Ms
~100 yellow M&Ms
3-4 plastic cups
7 students

Management

Estimated Time: 1 hour 30 minutes

Maximum Cost: $25

Safety Considerations

As the activity uses chocolate candies, identify students with this food allergy. Another colored candy may be substituted, and students do not need to eat the candy in order to understand the lesson. Do not conduct this demo in the laboratory, but rather move to an open classroom, hallway, or courtyard. You need a space only about 5m X 5m.

Before you start

Pour blue M&Ms into one of the bowls.

Pour green M&Ms into another one of the bowls.

Fill two jars half-way with yellow M&Ms.

Get Started!

1. **Facilitate student review of neurotransmission.** (Hit these highlights: Synthetic enzymes for neurotransmitters are made in the cell body, transported to the axon terminal via microtubules, and react with chemical precursors to make neurotransmitters. When an action potential arrives at the terminal, neurotransmitters are released and bind to postsynaptic receptors. Degradative enzymes break down neurotransmitters in the synapse.)

2. **Recruit volunteers for the following roles.** (Students can make necklace cards or hats with these abbreviations to remind them of their roles.)

Cell Body (CB): Holds blue M&Ms (synthetic enzymes)

Microtubules (M): Transports blue M&Ms (can be more than one)

Axon Terminal (A):	Holds yellow M&Ms (precursors) Releases green M&Ms (serotonin)
Receptor (R):	Receives green M&Ms (serotonin)
Action Potential (AP):	Triggers green M&M release
Degradative Enzyme (Z):	Destroys green M&Ms (serotonin)
MDMA (E, for ecstasy):	Gives green M&Ms (serotonin) in mass quantities to R.

3. Facilitate student review of specific duties. (Make diagrams, note cards, or additions to their necklace cards. See Fig. 4.)

4. Places please: Ask volunteers to stand in their places, according to Fig 4. (We have enjoyed placing stage directions on colorful cut-outs on the floor.)

5. Ask other student aides to place props.

a. Place the bowl of blue M&Ms in front of the cell body (Student CB).
b. Give two empty jars to the microtubule student(s) (M).
c. Place the bowl with the green M&Ms and the jars with yellow M&Ms in front of the terminal (A).
d. Place an empty bowl in the hands of degradative enzyme (Z) and ask the receptor (R) to hold the funnel over the bowl.

6. Let's Play!

Normal (Drug-Free) Neurotransmission

a. The blue M&Ms in the bowl, held by Student CB, represent the enzymes made by the cell body. The yellow M&Ms in the jars held by Student A, represent the precursors present in the axon terminal.

b. Students M (microtubules) carry enzymes to the axon terminal (Student A) in a jar filled halfway with blue M&Ms (synthetic enzymes).
c. Student M will then pour the blue M&Ms into the jar with yellow M&Ms (precursors).
d. Explain to the students that as the enzymes (blue M&Ms) react with the precursors (yellow M&Ms), the neurotransmitters (green M&Ms) are synthesized. (Just as mixing the colors blue and yellow makes the color green.) Shake the jar with blue and yellow M&Ms to represent synthesis, then place the jar into the bowl with green M&M. Use green M&Ms from here on; serotonin is ready.
e. For a neuron to communicate, an action potential travels from the cell body to axon terminal and signals neurotransmitter release. Student AP (action potential) walks from the cell body (Student CB) to the axon terminal (Student A) and tap Student A on the shoulder. Student A (axon terminal) then takes some green M&Ms and pours them through the funnel held by Student R (receptor). This funnel represents a binding site. The neurotransmitters (green M&Ms) fall through the funnel into a bowl, held by Student Z (degradative enzyme).
f. The degradative enzyme (Student Z) takes the neurotransmitters (green M&Ms) from the bowl and degrades them by eating them (!) or giving them to other students to degrade (eat!). (Alternatively the M&Ms can be placed in a trash receptacle to represent inactivation.)
g. Repeat as often as you like.

Ecstasy is Agony

a. Plan to repeat the sequence again, but this time ask MDMA (Student E) to grab handfuls of green M&Ms (serotonin) from the bowl in front of the axon terminal (Student A) and dump them into the degradation site.
b. Once the bowl with the serotonin (green M&Ms) is empty, the axon is destroyed; Student A sits down. Once Student A sits down, Student(s) M also sit(s) down. These events represent the degradation of the serotonin axon terminal and axon.
c. Ask students whether or not neurotransmission can occur when the axon terminal and axons are destroyed. (The answer is no.)

Assessment and Wrap-Up

In order to assess student learning, we administered a short quiz before and after the activity (Fig. 5). We tested the basics of neural function and asked whether students understood that MDMA alters nervous system activity. Make this a favorite activity in your class by reading our instructions, visiting the National Institute on Drug Abuse website, and enlisting your students to act out the effects of MDMA on the nervous system. Students will take away a lasting understanding of MDMA through your link with the memorable M&MDMA activity.

Acknowledgements

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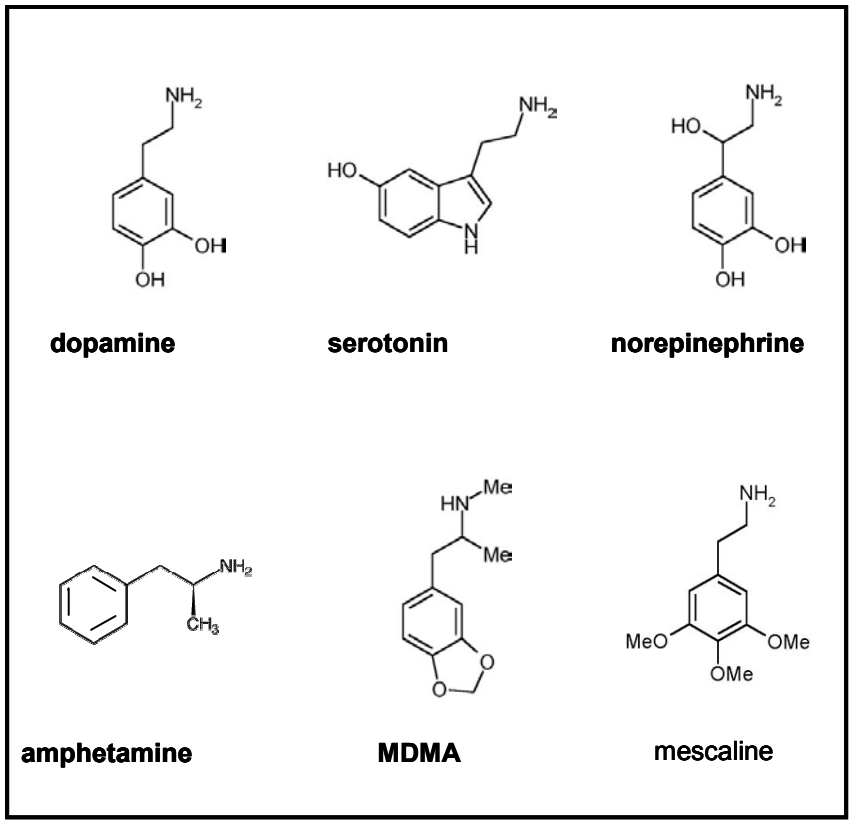
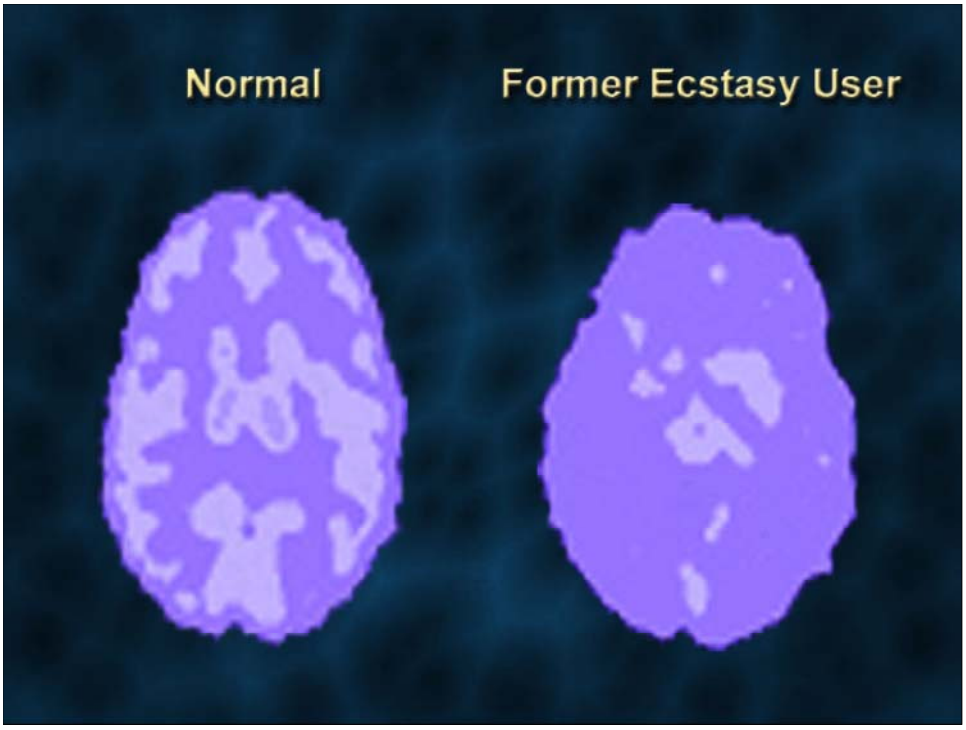
Figures

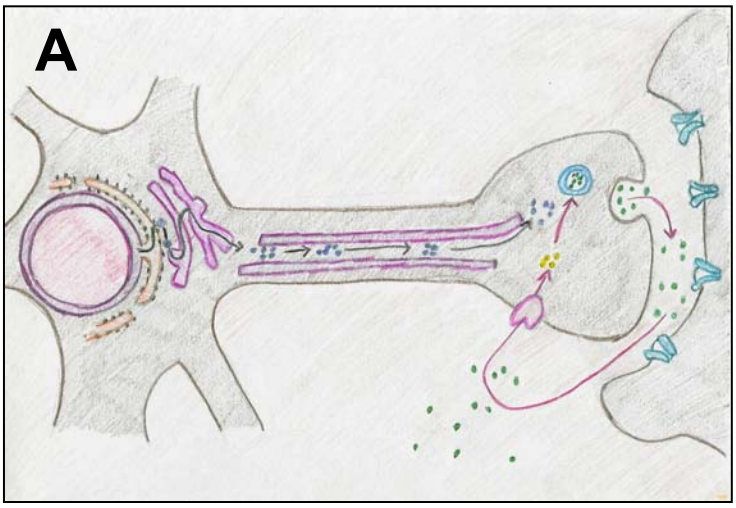
1. Molecular Structures of Neurotransmitters and Drugs. Similarities in structure between neurotransmitter molecules (top row) and drug molecules (bottom row) enable drugs to interfere with normal neurotransmission.

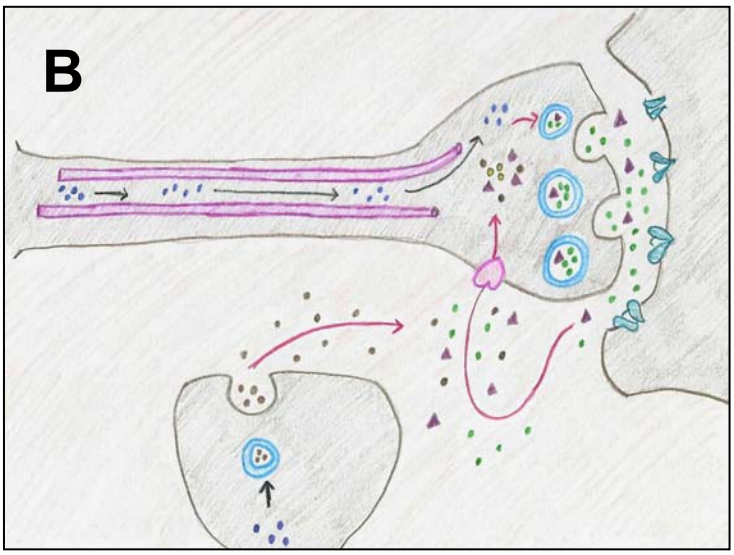


2. Positron Emission Tomography (PET) scans from a study comparing drug-naïve control humans with MDMA-experienced humans to show decreases in serotonin-related activity in the brain. (See www.nida.nih.gov Slide Teaching Packets for more information.)

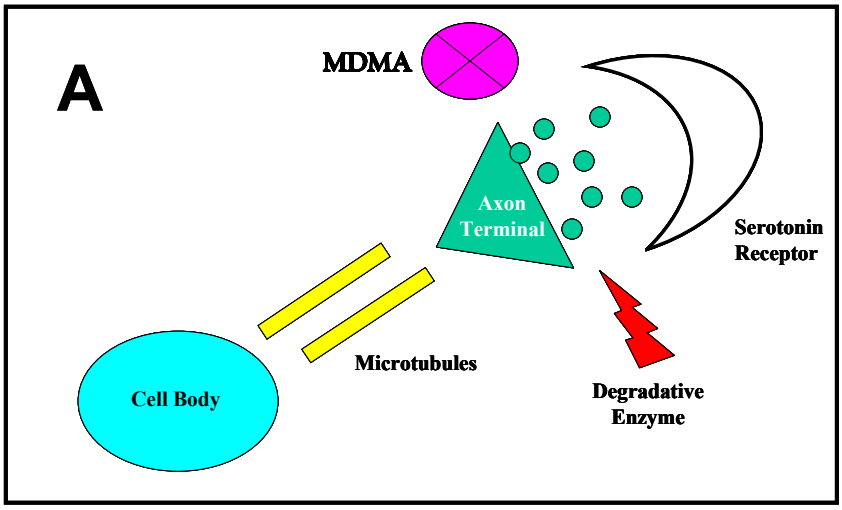


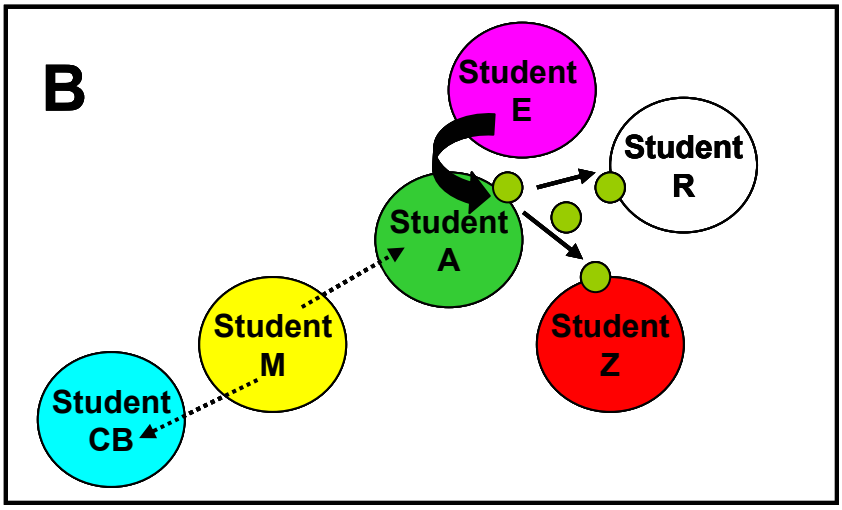
3. Neurotransmission: with and without MDMA. In panel A, synthetic enzymes (blue dots) are synthesized in the cell body, then carted on microtubules (long pink tubes) to the axon terminal. The synthetic enzymes catalyze reactions changing precursor molecules (yellow dots) into neurotransmitter molecules, such as serotonin (green dots), which are packaged into synaptic vesicles. Action potentials arriving at the axon terminal cause neurotransmitter release into the synaptic cleft. Neurotransmitter molecules encounter and bind to postsynaptic receptors (blue cones). Later, neurotransmitters can be taken back up into the nerve terminal via reuptake transporters (pink cones) or broken down by degradative enzymes (not shown). In panel B, MDMA molecules (purple triangles) are taken up into the nerve terminal via reuptake transporters (pink cones), where they move into synaptic vesicles and force neurotransmitters out into the synaptic cleft. Furthermore, MDMA increases dopamine release (brown dots), which contributes to degradation of serotonin terminals.





4. Schematic Diagram of M&MDMA. In panel A, the structures and molecules in neurotransmission are laid out. In panel B, we assign students to their places and indicate that Student M (microtubule) shuttles back and forth between Student CB (cell body) and Student A (axon terminal). Student A releases serotonin (green M&Ms) to Student R (receptor) who filters them through to Student Z (degradative enzyme). Student E (ecstasy/MDMA) grabs serotonin from Student A by the handful and gives them to Students R and Z. Student Z degrades the serotonin (eats the M&Ms).





Annotated Bibliography of Helpful WebSites

http://www.brainsrule.com

Website of the Brains Rule! Neuroscience Exposition project. Provides games for learning about the nervous system, as well as resources for teachers and neuroscience professionals.

http://www.cbn-atl.org

The Center for Behavioral Neuroscience (CBN) in Atlanta, Georgia, provides a more detailed description of this activity, information about neuroscience research, and a lending library of neuroscience-related materials to borrow for classroom use.

http://www.monitoringthefuture.org

Provides statistics on the use of a variety of illicit and legal drugs, among U.S. middle and high school students, with downloadable graphs and charts.

http://www.nida.nih.gov

Under "Information for Parents and Teachers", easily downloadable slide teaching packets and scripts are available. This is the National Institute on Drug Abuse website; it also describes drug effects and related problems in the Infofax, Community Drug Alert Bulletin, and Sarah Goes to School modules.

http://www.samhsa.gov

Free publications are available to order here, under the Addiction Treatment section from the Substance Abuse & Mental Health Services Administration of the U.S. Department of Health and Human Services. Also available are links for teens, news, and resources on treatment.

Annotated List of Sources Used for Introductory Material

Burgess, C., O'Donohoe, A., & Gill, M. (2000) Agony and ecstasy: a review of MDMA effects and toxicity. European Journal of Psychiatry 15: 287-294. The title of this article conjoins the terms "agony" and "ecstasy", so we give credit to its authors when we use the phrase "the agony of ecstasy". The article uses technical language to detail consequences of MDMA use.

Carey, J. (Ed.) (2002) Brain Facts. The Society for Neuroscience and The Everbest Printing Company, China. Primer on the brain appropriate for students beyond junior high. Available on-line at www.sfn.org.

Gudelsky, G.A. & Yamamoto, B. K. (2003) Neuropharmacology and Neurotoxicity of 3,4-Methylenedioxymethamphetamine. Methods in Molecular Medicine 79: Drugs of Abuse: Neurological Reviews and Protocols. Wang, J.Q. Ed. Humana Press Inc. Totawa, NJ. Highly technical description of research on effects of MDMA on the nervous system of animals.

Purves, D., Augustine, G.J., Fitzpatrick, D., Katz, L.C., LaMantia, A.-S., McNamara, J.O., & Williams, S.M. (2001) Neuroscience. Second Edition. Sinauer Associates, Inc. Sunderland, MA. A great addition to the personal library of any scientist of the brain and behavior.