**Reducing the stigma of depression**

grade level(s): 9-12 subject(s): Biology, anatomy & Physiology

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**Problem Statement:** Sara is a 11th grade high school student who is enrolled in several honors and AP classes. She is a conscientious student, normally earning As and Bs. While she maintained an honor roll GPA for first semester, she has missed many days of class second semester and her grades are slipping. She returned to class after a 3 day absence and during lunch her friend Taylor asked her where she had been. At first Sara said she had the flu, but when Taylor expressed concern, Sara broke down. She swore Taylor to secrecy, confiding that she had been feeling that her life was worthless and could not get out of bed some days. Sara said that some days it had been so bad that she had considered ending her life. Sara swore up and down that she was feeling much better and begged Taylor not to say anything to anyone. Taylor does not want to break the trust Sara has in him and promises not to say anything to anyone.

Two youths between 10 and 24 years of age die by suicide each week. While not all people with depression commit suicide, nearly all suicide is related to depression or other mental illness. Seventy percent of those who commit suicide communicate this intention to others. Your school district has written a grant and has money to spend on addressing this problem. They have asked you, as teams, to research what is currently being done to address depression. and develop an action plan to decrease the stigma associated with depression. You will present your action plan to representatives of the school board and carry out your plan.

In this lesson, we will uncover students’ current understanding and experience with depression. Students can revisit the chalk talk periodically through the unit as a measure of how their conceptions are changing with new and deeper understanding.

**Conceptual Storyline:**

After being introduced to a fictitious scenario regarding a teenager suffering from depression (see problem statement), students will explore their own conceptions/misconceptions regarding depression through a silent chalk talk. The chalk talk will be revisited throughout the unit as students explore the topic.

Through a series of simulations, role plays, and discussion activities, students will understand how the brain functions through neurotransmission, how neurotransmission can be altered in people with depression, potential genetic components, and external factors that may contribute depression.

Once students have an understanding of depression as a medical conditions, we will revisit the problem of youth struggling with depression. Students will be placed on teams to develop an action plan aimed at reducing the stigma associated with depression. Action plans will be presented to the class. At teacher discretion, the ‘winning’ action plan can be implemented by the class, or all action plans that are feasible and meet standard can be implemented.

**Unit Standards (NGSS, CCSS, CTE):**

NGSS HS-LS1-2. Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms.

NGSS HS-LS3-1. Ask questions to clarify relationships about the role of DNA and chromosomes in coding the instructions for characteristic traits passed from parents to offspring.

NGSS HS-LS4-3. Apply concepts of statistics and probability to support explanations that organisms with an advantageous heritable trait tend to increase in proportion to organisms lacking this trait.

What standards (content and practices) are you addressing in this unit/lesson(s)?

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CCSS ELA HS

**21st Century Skills:**

Collaboration, Communication, Presentation Skills

**Locally and/or Personally Relevant for Students:**

Students will learn about resources currently available in their schools and communities. The students will gain knowledge of the physiological and environmental causes of depression.

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LESSON 2: Neurotransmission and the Brain - Through an interactive presentation, students learn the basics of how messages are transmitted in the brain.

LESSON 3: Neurotransmission Role Play - Students model a simple nerve circuit, both functioning normally and with disruptions that could cause depression.

LESSON 4: Using Genomics to Find the Right Medicine - Students use tools of bioinformatics to determine patients’ drug metabolism phenotype, then determine how to adjust their depression medication.

LESSON 5: Grant Proposal and Action Plan - Student teams propose ideas to address and reduce the stigma associated with depression

SUPPLEMENTAL LESSON 6: Environmental Causes of Depression - Students brainstorm and address potential environmental triggers that can lead to depression.

**Lesson 1: Depression Chalk Talk**

**Learning Objectives:**

* Students will explore and share their thoughts on the nature of depression
* Students will self-assess the depth of their knowledge related to depression

**Lesson Standards (NGSS, CCSS, CTE):**

21st Century Skills:Collaboration, Communication, Presentation Skills

**Materials:**

* Access to scenario to read to the class
* Butcher paper or giant sticky notes
* Multiple colors of markers
* Copies of images for posters
* Ability to project chalk talk rules or whiteboard to write them on.
* Tape or thumbtacks for hanging posters.

**Lesson Preparation:**

1. Reproduce chalk talk posters (Teacher Resource 1.1). Using large pieces of butcher paper, reproduce the images as shown in the chalk talk poster templates. Words/statements should be relatively small so that there is adequate white space for students to record their thoughts and respond to others.
2. Print copies of images for chalk talk posters, or draw similar images on appropriate posters.
3. Hang posters on walls, distributed throughout the room, prior to class beginning.
4. Distribute markers so a few are available at each poster.
5. Project chalk talk rules (Procedures, Brainstorm: a-h) or copy rules and tape next to each poster.

**Time Required:**

Approximately 30 minutes.

**Grouping of students for instruction:**

Students will work independently for this activity. They may travel between posters as they choose.

**Procedure:**

**Introduction/Problem Launch**

1. Teacher will read the introductory fictitious scenario. After reading it to the class, take questions and comments from the class.
2. The purpose of this activity is just to generate interest and allow students to understand the relevance of the topic. Teacher should refrain from attempting to ‘teach’ at this time, but rather allow students to generate questions and share experiences and thoughts.

**Brainstorm What Students Know/Need to Know**

1. Draw students’ attention to the posters. Tell them they will engage is a **silent chalk talk**. Review the rules of chalk talk:
   1. Respond to the main comment anywhere on the poster you like.
   2. Respond to other by drawing an arrow from their comment to yours
   3. Keep all responses respectful and school appropriate
   4. If you agree with a statement add an asterisk or exclamation point (\*!)
   5. If you disagree, with something that someone says, explain why you disagree using appropriate language.
   6. Do not cross out or write over anything anyone writes.
   7. Pictures are completely permissible as long as they are appropriate.
   8. **NO TALKING!!**
2. Read each of the posters and explain how to mark their location on the grid.
3. Tell students that they must respond at least once to each of the main prompts on each of the posters. Then they should read the comments others have written and respond to at least one comment on each poster.
4. Remind them there is to be no talking and allow ~30 minutes for them to participate in the chalk talk.
5. When students are done and have returned to their seats, tell them that they are not to talk about the posters or comments until you debrief at the end of unit.
6. Leave the posters up for the duration of the unit. You may have students revisit the posters as you complete lessons throughout the unit.

**Follow up:**  Before introducing the final project,debrief the chalk talk.

1. Give students 5-10 minutes to record any final thoughts on any of the posters
2. Discuss each poster one by one. Ask students:
   1. What were your original ideas about this prompt?
   2. Did your ideas change?
   3. How did they change?
3. Specifically address the science concepts related to the poster “What is happening in a person’s brain to make them feel happy or sad” to reinforce the biological processes learned in class. Correct any misconceptions and clarify any confusion.
4. Discuss the poster with the cartoon lask. Ask students ‘What is wrong with just telling someone with clinical depression that they should stop being sad?” Students should be able to describe how there are biological mechanisms that are not under the person’s control. Clarify and correct any misunderstanding.

**Assessment:**

Student responses will serve as the assessment to this lesson.

**Accommodations:**

Ensure that posters are at a height and location accessible to all students. If students have computers, posters could be electronic, with student participating via google doc, etc.

**Extensions:**

Follow the silent chalk talk with lesson 2 from NIH - The Science of Mental Illness (PDF files)

Revisit posters following completion of each lesson. Allow students to add new ideas as they get new information. Remember, older ideas must not be crossed out/removed.

**Lesson number 2**

**Neurotransmission and the Brain-An Introduction**

**Learning Objectives:**

* Students will be able to describe the meaning of the term neurotransmission.
* Students will be able to describe why neurotransmitters are necessary.
* Students will be able to describe the basic anatomy of a neural connection.
* Students will be able to describe a possible genetic link to depression

**Lesson Standards (NGSS, CCSS, CTE):**

HS-LS1-2 Molecules to Organisms -- Structure and Processes (model)

Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms. [Clarification Statement: Emphasis is on functions at the organism system level such as nutrient uptake, water delivery, and organism movement in response to neural stimuli. An example of an interacting system could be an artery depending on the proper function of elastic tissue and smooth muscle to regulate and deliver the proper amount of blood within the circulatory system.] [Assessment Boundary: Assessment does not include interactions and functions at the molecular or chemical reaction level.]

Number and Quantity NQ.2

Reason Quantitatively and Use Units to Solve Problems. Define appropriate quantities for the purpose of descriptive modeling.

Number and Quantity NQ.3

Choose a level of accuracy appropriate to limitations of measurement when reporting quantities.

Algebra A-SSE.1\*

Seeing Structure in Expressions. Interpret the structure of expressions. Interpret expressions that represent a quantity in terms of its context.

Statistics and Probability S-IC.1

Making inferences and Justifying Conclusions. Understand and evaluate random processes underlying statistical experiments. Understand statistics as a process for making inferences about population parameters based on a random sample from that population.

**Materials:**

* Laptop computer or paper note taking ability
* Lesson 2 Worksheet
* Lesson 2 Article “# Life Unfiltered”

**Lesson Preparation:**

1. Read over the entire lesson. Check the links in the Powerpoint
2. Prepare copies of the Worksheet and the Article
3. #Life Unfiltered should be read prior to class

Time Required: Two-50 minute periods if “#Life Unfiltered” is read out of class, three 50 minutes periods if read in class.

**Procedure:**

***Understand The Problem:***

What is the anatomical and physiological basis of how do neurons communicate with each other?

What is the function of brain chemicals?

What may be the effects of abnormalities of neurotransmission

**Further Extensions:**

On the board--What would happen if one of the dendrites did not work? Axons? Terminal fibers? What could happen if a dendrite did not recognize the specific neurotransmitter?

**Assessment:**

Exit Ticket, to be completed by each student upon exit of class. The Lesson 2 worksheet will be turned in at the end of class.

**Accommodations:**

No accommodations outside of normal lecture accommodations needed

**Lesson #3: Neural Transmission Activity**

**Learning Objectives:**

* Students will enact a presynaptic neuron as it releases neurotransmitters.
* Student will understand the activation of receptors on a postsynaptic cell.
* Students will synthesize that neurotransmitters related to depression-- dopamine, norepinephrine, and serotonin-- operate exclusive from one another through specific receptors, and that without these neuroreceptors there will not be neural synapse.

**Lesson Standards (NGSS, CCSS, CTE):**

HS-LS1-2 Molecules to Organisms -- Structure and Processes (model)

Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms. [Clarification Statement: Emphasis is on functions at the organism system level such as nutrient uptake, water delivery, and organism movement in response to neural stimuli. An example of an interacting system could be an artery depending on the proper function of elastic tissue and smooth muscle to regulate and deliver the proper amount of blood within the circulatory system.] [Assessment Boundary: Assessment does not include interactions and functions at the molecular or chemical reaction level.]

**Materials:**

* 10-20 copies of + / – paper sheets to represent movement of charged atoms (Handout 3.1)
* 1 copy of Happy/Sad Emoji Card for last person in series, with role of Human Emotion (Handout 3.2)
* Student readings for activity roles--see groupings below for amounts (Handout 3.3)
* Class copy set of Neuron Anatomy/Synaptic Gap Images (Handout 3.4)
* Neural Activity Questions worksheet for students (Handout 3.5)
* 6-8 hard objects to be hand-held in Part III, such as tennis balls or building blocks
* EXTENSION-2-3 kinds of wrapped, hard candies to represent different neurotransmitters

**Lesson Preparation:**

1. Read over the entire lesson. Determine what you will use for 3 different types of candies, to symbolize neural transmitters.
2. Form groups for the activity. Make 3 neurons, minimum 10 students each (see below).
3. Make appropriate number of copies of Student Handouts 3.1-3.5.
4. Redesign your room. Offer space for students to form neural cells. OPTION: stage classroom with tables in 3 rows (3 neurons). Tape student readings for activity roles to table/seats (Handout 3.4). Ensure last seat ends with Emotion instruction.

**Time Required:** One-50 minute period

**Grouping of students for instruction:**

Divide class into 3 “neurons”, minimum 8 students each

* 1-2 people will serve as Dendrites (Handouts 3.2, 3.3)
* 6-8 students as Axons (Handouts 3.1, 3.4)
* 1-2 students as Axon Terminals (Handouts 3.2, 3.3)

Each student will be given a specific handout (3.3-3.4) describing their specific role as parts of their neuron. They should be given time to discuss their role with others of the same role before the simulation starts (5”) OR taping handouts to tables.

**Procedure:**

***Understand The Problem:***

**Part 1---Why do we care? Chalk Talk #2 (5-15”)**

(OPTION) have students review Chalk Talk norms, revisit comments. Do they have anything to add?

**Part 2---Neural Transmission Activity (35-45”)**

Hand out Neural Activity Questions worksheet for students (Handout 3.8). Have students quietly answer the first two questions, then classroom discuss:

**1. What are the rules to the game "Telephone"?** Engage students on how telephone works, to relate neural transmission communication.

**2. Why is the message in telephone rarely communicated correctly?**

Hand out Class Copies of Neuron Anatomy/Synaptic Gap Images (Handout 3.7). Discuss: What are the parts to a neuron? What do they do? What is a synapse?

**3. How do neurons and dendrites work together to forge neural communication?**

To make the connection from the lesson on the anatomy of the brain, students will watch the following clips:

NG: Mapping the brain (22min-- first 5-6 minutes clip)

<https://www.youtube.com/watch?v=7_drJyNMXbw>

*Annotation: this clip is visually appealing, with easy to understand images of the brain and neural connections. Interesting research on current-day knowledge.*

NG: real neurons (5min)

<https://www.youtube.com/watch?v=nvXuq9jRWKE>

*Annotation: this clip gives more detail into the anatomy of neurons.*

***Explore the Problem:***

**4. *What initiates activation? How does the neuron release a NT? Where does the NT go?***

*Pre-Activity*

1. Show Animation: general neurotransmitter synapse (first 30 seconds)
   1. <https://www.youtube.com/watch?v=90cj4NX87Yk>
   2. Instruct axons how to use +/- cards to show communication. What does it look like? (a wave, sporting event, lit fuse, etc). Have students demonstrate understanding by modeling this.
2. Show the rest of the Animation. Ask students: what part are Axon Terminals? Dendrites? What are they producing? Why? What will this do?
3. Model how Axon Terminals will hand Neurotransmitters (candy) to Dendrites, and how that will start Action Potential.
4. Ensure that the final end will know to hold up Emoji Card Happy Face when/if communication reaches them.

*Activity: Phase 1-- Neurons in a series*

1. (IF YOU DO NOT HAVE TABLES SET UP AS NEURONS) Students form one of the 3 neurons, each role is represented by a/many student(s). Check for accuracy of their form.
2. TO BEGIN: Teacher tosses some candy toward the receiving Dendrite(s) of Neuron #1.
3. Once the “message” has been received--it reaches threshold, the first part of the “Axon” flips their sign sheet from - to + (or makes a plus-sign with their arms and then drop their arms back down like a wave).
4. Subsequent Axons continue the above and it goes down the line.
5. The Axon Terminal(s) hand their candy to the Dendrite(s) of Neuron #2. The ending axon terminal show Happy Face Emoji card to show the communication was complete.

*Activity: Phase 2--Neurons in a Series*

1. What happens to information transmission when there is not enough neurotransmitter chemicals to initiate communication?
2. What will happen if a dendrite is unable (blocked from) uptake of neurotransmitters?
3. 2 runs:
4. 1st run-- instruct students that there will only be one NT candy at the dendritic site (or not enough). Result: Communication will cease-- axons will not display + cards, terminals will not display “I am happy!” cards.
5. 2nd run--offer the dendrites tennis balls/building blocks, so that they have large objects in each “dendritic receptor” hands. Toss some NT candy toward receiving dendrites. Result: dendrites cannot hold/manage the NT candy, so communication will cease-- axons will not display + cards, terminals will not display “I am happy!” cards.

*EXTENSION---Activity: Neurons in a Series*

**On the board--*Are there other neurotransmitters involved in the transmission of information?***

1. Assign first neuron to pass dopamine “candy NT” as before.
2. Assign second neuron to norepinephrine “candy NT”, designating dendrites, axon terminals to only receive/pass norepinephrine candy only.
3. Assign third neuron to Serotonin “candy NT”, instruct the same process as #9.
4. Run simulation by putting specific candy with specific dendrites. Neurons will respond to candy, axons will reach Threshold and display + cards, terminals will display “I am happy!” cards.

**Further Extensions:**

On the board--What would happen if one of the dendrites did not work? Axons? Terminal fibers? What could happen if a dendrite did not recognize the specific neurotransmitter?

Have student read the article “What causes depression” and answer the questions (L3 - What causes depression reading).

Follow with Lesson 3 from NIH - The Science of Mental Health (PDF files)

**Assessment:**

Exit Ticket, to be completed by each student upon exit of class. 3-4 questions, project on doc camera/projector/whiteboard.

1. How do neurons and dendrites work together to forge neural communication?
2. What initiates activation? How does the neuron release a NT? Where does the NT go?
3. Are there other neurotransmitters involved in the transmission of information?
4. What would happen if one of the Dendrites did not work? Axons? Axon Terminals?
5. What could happen if there is not enough neurotransmitting chemicals to initiate communication?
6. How was neurotransmission altered in this simulation? What result did this have?
7. How is this alteration similar to that of someone with depression? What result could/would this have?

**Accommodations:**

Students who are visually/physically impaired can perform activity with cell parts that require more than one student, ie. dendrites, axons, axon terminals

**References/Resources:**

See handouts, videos above

**Lesson Four: Using Genomics to Find the Right Medication**

**Learning Objectives:**

* Learn how mutations in a patient’s DNA can affect how they metabolize medication
* Understand and perform the clinical process for discovering and annotating mutations, including working with variant call format files commonly used in bioinformatics pipelines
* Think about how metabolic rates can affect the type of medication a patient should be prescribed

**Lesson Standards (NGSS, CCSS, CTE):**

HS-LS1-2 Molecules to Organisms -- Structure and Processes (model)

Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms. [Clarification Statement: Emphasis is on functions at the organism system level such as nutrient uptake, water delivery, and organism movement in response to neural stimuli. An example of an interacting system could be an artery depending on the proper function of elastic tissue and smooth muscle to regulate and deliver the proper amount of blood within the circulatory system.] [Assessment Boundary: Assessment does not include interactions and functions at the molecular or chemical reaction level.]

**Materials:**

* Computer with access to the internet
* Each student or group of students will need to download one of three variant call format (VCF) files:
  + [**Patient 1: Jessica Jones**](https://drive.google.com/open?id=0B7KVqGSfimzWQkNtN3llOFZmNjA)
  + [**Patient 2: Matt Murdock**](https://drive.google.com/open?id=0B7KVqGSfimzWazZfSWU2OUgxY0E)
  + [**Patient 3: Wade Wilson**](https://drive.google.com/open?id=0B7KVqGSfimzWLXktM3J2Y25iZkU)

**Lesson Preparation:**

1. Make sure that student can access the following website:  
   <http://wannovar.usc.edu/>
2. Download the VCF files to a location that the students will have access to. Each student (or group of students) will need to download one of the patient VCF files.
3. Update link locations to VCF files in the following documents:   
   - Student Protocol: under section "Collect Patient VCF files from sample analysis"  
   - Teacher’s handout
4. Optional: Place patient reports in manila envelope marked confidential
5. Students should receive the following documents:
   1. Student handout: Provides step-by-step directions and review questions for each step
   2. Patient Reports: Fictitious patient background and place to write down results of metabolic assessment and treatment plan recommendations
   3. Journal Article: Provides needed background information
   4. Protocol: Step by step directions for annotating VCF files
   5. Patient Report Summary: A summary sheet that students will hand in at the end of the lesson
   6. Lesson 4 Concluding Statement: The overall lesson summary that students should turn in at the end of the lesson
6. Optional: Walk students through the introductory scenario provided in the Student Handout
7. Walk students through the background PowerPoint presentation located [here](https://docs.google.com/a/msvl.k12.wa.us/presentation/d/1gqgpUUDNiBWu4An-H_LGTr_-iiEfQiSMoSw5nK6p_lk/edit?usp=sharing).
8. Optional: Walk students through the background information contained in the journal article

**Teacher Tips:**

* Students will attempt to open the VCF file in Excel, and this will only work if you import the file manually. Warn them not to open the file.
* On some operating systems, such as Windows 7, the file may automatically download as a VCard, and will not work properly in wAnnovar. If this happens:
  + Right click on the VCF file
  + Choose “Open With”
  + Browse to the location of Microsoft Excel on your computer (check your Microsoft Office folder)
  + Select the option to always have Excel open this file type
  + Try uploading the file again
* If students have trouble linking the annotated VCF results to a treatment plan, tell them to look at the Clin\_DIS column
* It can take a long time for the VCF annotation results to arrive by email. If this happens, there are backup versions available for download in the Patient VCF files folder:   
  https://drive.google.com/open?id=0B7KVqGSfimzWNFhreU9nMlM0UUU

**Time Required:**

60 minutes

**Grouping of students for instruction:**

It is up to the teacher whether or not the students should work in groups or together, depending on computer access and time constraints. Each of the three patient VCF file should be randomly distributed between students or groups.

## **Lesson Goal:**

After the VCF file is generated, variant annotation software is used to compare any mutations found against a number of databases to determine if the mutation is known to be linked to any particular disease.

# **Background:**

The CDC estimates that 40-50% of patients diagnosed with clinical depression do not respond to drug therapy, while many more must try several different medications before finding an effective treatment. Genetic testing of depressed patients has found that variations in the cytochrome p450 system, a family of isozymes responsible for the metabolization of drugs, can affect how a person’s body responds to different treatments.

Isozymes are enzymes that differ in amino acid sequence, but catalyze the same chemical reaction. Although there are more than fifty p450 isozymes, there are six main enzymes that play a role in drug metabolism, two of which have been shown to have a strong link to clinical depression; CYP2D6 and CYP2C19.

Discovering how a patient’s metabolism works can help determine the best type of treatment for them, as well as prevent an adverse drug reaction (ADR).

## **Four Metabolic Phenotypes**

Scientists have identified four main phenotypes of metabolizers (Serani, Deborah 2014):

* **Poor metabolizer (PM):** person who metabolizes the medicine very slowly. The medicine can build up in this person’s system, causing severe side-effects and toxicity.
* **Intermediate Metabolizer (IM):** a person whose metabolism is slower than a normal person. They still run the risk for side effects and toxicity, but not as much as a PM.
* **Extensive Metabolizer (EM):** These people metabolize drugs in a normal way and tend to experience relief of their symptoms with little to no side effects.
* **Ultrarapid Metabolizer (UM):** These people process medication so quickly that the treatment has no effect.

## **CYP2D6**

**Location**: chromosome 22q13.1

CYP2D6 is an enzyme primarily expressed in the liver. Responsible for the metabolization of more approximately 25% of clinically used drugs.

## **CYP2C19**

**Location:** chromosome 10q23.33

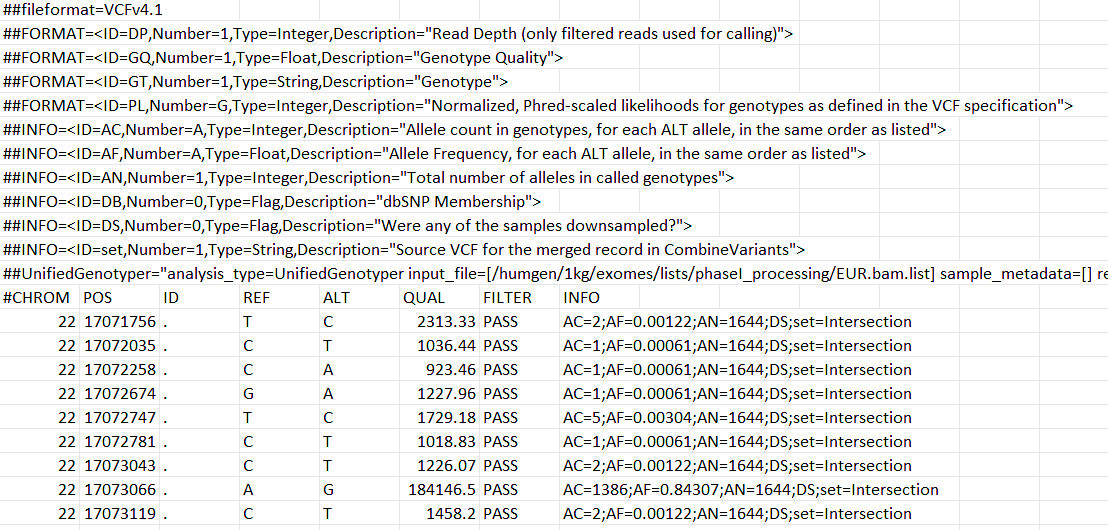
CYP2C19 is an enzyme primarily expressed in the liver. Responsible for the metabolization of approximately 10-15% of clinically used drugs, including antidepressants and benzodiazepines.

## **Mutations and the Variant Call Format (VCF)**

Next generation sequencing (NGS) is used to determine if a particular region of a person’s genome contains any mutations that might alter the protein products produced in this region.

The process of SNP calling begins with a clinician or researcher taking a sample of the patient’s DNA. Computer software is then used to compare that patient’s DNA sequence to that of a reference sequence, determining if that person’s sequence is different from the reference, indicating that there may be a single nucleotide variants (SNV’s), insertion or deletion (indel) that would cause an alteration in the protein product produced by the region of interest.

The output of SNP calling is called a VCF file, that looks similar to the file shown below:



This might look complicated, but here’s what it all means:

* Each line that begins with a ## is for informational purposes and describes the type of information put into the FORMAT and INFO fields.
* CHROM = the chromosome where the variant was found
* POS = the genomic position where the variant was found
* REF = the nucleotide in the reference genome
* ALT = the mutated sequence found in the patient
* QUAL = a quality score reflecting how sure the software is the the variant call is correct
* FILTER = indicates if the variant call pass a number of filtering tests
* INFO = this can change with each VCF file and usually described in the header in each line beginning with a ##

# **Introducing the Activity to Students**

The student handout introduces the following scenario:

Congratulations! You have been awarded a summer internship at the Willamette Valley Health Center with Dr. Funke, a well-respected psychiatrist who specializes in the treatment of severe depression. On your first day, Dr. Funke asks you to assist him in reviewing treatment plans for three patients who have had genetic testing to determine if they have mutations in two gene regions that could affect the way they metabolize medication; CYP2D6 and CYP2C19. This is a relatively new, and much-debated, test in the field of psychiatry, so Dr. Funke provides you with a journal article to read for background information, the files of three patients who have been having trouble with medication and a protocol to follow for completing the assessment.

After reviewing the patient files, read the journal article Dr. Funke gave you, and select a patient you would like to review. Then follow Dr. Funke’s protocol to assess whether or not you think Dr. Funke will need to adjust the patient’s medication.

**Activity**

After reading through the abridged journal article and patient records, the students will pick one of three simplified VCF files representing the patient they want to analyze. Each simplified VCF file represents a patient with a mutation in either the CYP2D6 or CYP2C19 gene regions, as shown in the chart below:

|  |  |  |
| --- | --- | --- |
| **Patient** | **Mutated Allele** | **Phenotype** |
| Patient 1: Jessica Jones | CYP2D6\*2 = increased function | Ultra Rapid Metabolizer (UM) |
| Patient 2: Matt Murdock | CYP2D6\*3 = loss of function | Poor Metabolizer (PM) |
| Patient 3: Wade Wilson | CYP2C19\*4= loss of function | Poor Metabolizer (PM) |

The students will use an online variant annotation tool to determine what type of mutation their VCF file contains, and then use this information to discuss how this might affect that patient’s response to anti-depression medication.

# **Lesson Instructions**

1. Provide students with copies of each patient’s psychological assessment (if you can put these in a manila envelope that says “Confidential” that would make it more awesome):  
   <https://docs.google.com/document/d/1LmH51P_K6rM3zLIAEsdH5vPwJDJxE5gii9Ue0c7jaJc/edit>
2. Provide students with a copy of the protocol located at: <https://docs.google.com/document/d/1wrcFZJvNqwV9-KlfRyzYda11ZPGdC-7fGxgnTVxSY80/>
3. Provide students with a copy of the abridged journal article located at:   
   <https://docs.google.com/document/d/16G5YHSFaPB6_JmFMkbZo49jA4T2sF9v5hXzl5v-EUQg/edit>
4. Provide students with a copy of the Patient Summary located at:   
   <https://drive.google.com/open?id=14R_dcKcBhQsUK7yVGoXOtsq5kJ2z4YCYBx08-XGt3hI>
5. Provide students with a copy of the Lesson 4 Concluding Summary located at:   
   https://drive.google.com/open?id=0B5Uki\_uYXoucVXVwMW4zb0pIV3c
6. Have each student/group download one of the three patient VCF files:
   1. [Patient 1](https://drive.google.com/open?id=0B7KVqGSfimzWQkNtN3llOFZmNjA): Jessica Jones
   2. [Patient 2](https://drive.google.com/open?id=0B7KVqGSfimzWazZfSWU2OUgxY0E): Matt Murdock
   3. [Patient 3](https://drive.google.com/open?id=0B7KVqGSfimzWLXktM3J2Y25iZkU): Wade Wilson
7. Walk through the PowerPoint located at:  
   <https://drive.google.com/open?id=1gqgpUUDNiBWu4An-H_LGTr_-iiEfQiSMoSw5nK6p_lk>
8. You may want to walk students through the background information outlined above and in the abridged journal article, and introduce the patient stories provided at the beginning of their handout.
9. The VCF annotation results can take a long time to return. If you are running short on time, or if you have limited internet access, truncated backup copies of the annotation results can be found in the Patient VCF files folder:  
   https://drive.google.com/open?id=0B7KVqGSfimzWNFhreU9nMlM0UUU

**Assessment:**

Students will turn in a document answering the discussion questions at the bottom of their handout, as well as their recommendation for how they would alter their patient’s treatment based on the outcome of their analysis. Students will complete, and hand in, the Word Bank Summary.

**References/Resources:**

Centers for Disease Control and Prevention. (2015). CYP450 Genotyping to Predict Response to SSRIs Used to Treat Non-psychotic Depression in Adults: EGAPP™ Recommendation.

[http://www.cdc.gov/genomics/gtesting/EGAPP/recommend/CYP450.anthtm](http://www.cdc.gov/genomics/gtesting/EGAPP/recommend/CYP450.htm)

Chen, Qi, Zhang, Tao, Wang, Jing-Fang, Wei, Dong-Qing. (2011). Advances in Human Cytochrome P450 and Personalized Medicine. Current Drug Metabolism: State Key Laboratory of Microbial Metabolism, Luc Montagnier Biomedical Research Institute, and College of Life Sciences and Biotechnology, China

<https://www.researchgate.net/publication/50938518_Advances_in_Human_Cytochrome_P450_and_Personalized_Medicine>

Droll K, Bruce-Mensah K, Otton SV, Gaedigk A, Sellers EM, Tyndale RF (1998). "Comparison of three CYP2D6 probe substrates and genotype in Ghanaians, Chinese and Caucasians". Pharmacogenetics 8 (4): 325–33.[doi](https://en.wikipedia.org/wiki/Digital_object_identifier):[10.1097/00008571-199808000-00006](https://dx.doi.org/10.1097%2F00008571-199808000-00006). [PMID](https://en.wikipedia.org/wiki/PubMed_Identifier) [9731719](https://www.ncbi.nlm.nih.gov/pubmed/9731719).

<https://www.ncbi.nlm.nih.gov/pubmed/9731719>

S A Scott,1 K Sangkuhl,2 C M Stein,3 J-S Hulot,4,5 J L Mega,6 D M Roden,7 T E Klein,2 M S Sabatine,6 J A Johnson,8,9,10 and A R Shuldiner11,12,\*. Clinical Pharmacogenetics Implementation Consortium Guidelines forCYP2C19 Genotype and Clopidogrel Therapy: 2013 <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0048548/>

Serani, Deborah. (2014). Genetic Testing for Better Depression Treatment. Psychology Today.

[**https://www.psychologytoday.com/blog/two-takes-depression/201407/genetic-testing-better-depression-treatment**](https://www.psychologytoday.com/blog/two-takes-depression/201407/genetic-testing-better-depression-treatment)

**Lesson Number 5: Action Plan/Grant Proposal**

Problem Statement: Sara is a 11th grade high school student who is enrolled in several honors and AP classes. She is a conscientious student, normally earning As and Bs. While she maintained an honor roll GPA for first semester, she has missed many days of class second semester and her grades are slipping. She returned to class after a 3 day absence and during lunch her friend Taylor asked her where she had been. At first Sara said she had the flu, but when Taylor expressed concern, Sara broke down. She swore Taylor to secrecy, confiding that she had been feeling that her life was worthless and could not get out of bed some days. Sara said that some days it had been so bad that she had considered ending her life. Sara swore up and down that she was feeling much better and begged Taylor not to say anything to anyone. Taylor does not want to break the trust Sara has in him and promises not to say anything to anyone.

Two youths between 10 and 24 years of age die by suicide each week. While not all people with depression commit suicide, nearly all suicide is related to depression or other mental illness. Seventy percent of those who commit suicide communicate this intention to others.

Your school district has written a grant and has money to spend on addressing this problem. They have asked you, as teams, to research what is currently being done to address depression. and develop an action plan to decrease the stigma associated with depression. You will present your action plan to representatives of the school board and carry out your plan.

**Learning Objectives:**

Students will learn about resources currently available in their schools and communities.

Students will form action plans to decrease the stigma of depression in their communities.

Students will present their action plans, including rationale for why they believe it is the best course of action.

**Lesson Standards (NGSS, CCSS, CTE):**

CCSS ELA Writing HS W9 - 10.6. Production and Distribution of Writing. Use technology, including the internet, to produce, publish and update individual or shared writing products, taking advantage of technology’s capacity to link to other information and to display information flexibly and dynamically.

CCSS ELA Speaking & Listening SL9 - 10.4. Presentation of Knowledge and Ideas. Present information, findings and supporting evidence clearly, concisely and logically such that listeners can follow the line of reasoning and the organization, development, substance and style are appropriate to purpose, audience and task.

**Materials:**

Handout - Lesson 6 Action plan overview, template, roles, and rubric

Handout - Lesson 6 Group evaluation form

**Lesson Preparation:**

Day 1

1. Review what students have learned over the past several lessons. Prompt them to recall that depression is a medical illness with biological and chemical causes, yet many suffering do not seek or receive treatment.
2. Have students think silently about what misconceptions the general public (and high school kids in particular) hold about mental illness and depression. Help them define mental illness as needed.
3. After they have thought for 1-2 minutes, have partners brainstorm a list of as many misconceptions related to depression as possible, and record on a piece of paper.
4. After partners 5-7 minutes, have partners share with a larger group (4-6 total) and add to their lists.
5. As a class, compile ideas. Write “Misconceptions About Depression” on the board. Have one group volunteer to share one misconception and write it on the board. Proceed to subsequent groups, asking each to share one while you record on the board. Continue rotating through groups until all ideas have been mentioned.
6. Tell students that they are going to plan projects that will attempt to change these misconceptions and address the stigma associated with depression. Project the action plan overview/description and read to the class.
7. Show students examples of things that are already being done:
   1. <http://www.people.com/article/teen-candlemaker-generational-voice-for-those-battling-mental-illness>
   2. <https://stampoutstigma.com/>
8. Instruct student groups to brainstorm ideas for projects they could plan to reduce the stigma of depression and address misconceptions. Tell students that for the purposes of brainstorming all ideas should be recorded without judgment. Give student groups 15-20 minutes to brainstorm and research ideas.

Day 2

1. Handout student packets that contain the project overview, action plan template, scoring rubric and group member roles.
2. Review the goals of the project, the sections of the action plan/grant proposal, scoring rubric and student roles with the class.
3. Tell the class that they should now select the project their group wishes to pursue from the ideas they brainstormed previously, and select roles or each group member.
4. Make the action plan/grant proposal document available electronically so it can be completed electronically if computers are available.
5. Monitor groups to ensure they are proceeding satisfactorily and to answer questions as needed.

Day 3 and Day 4 - group work time.

Day 5 - Group presentations

1. Student groups will present and teacher grade presentation using rubric.
2. Student groups should turn in their completed action plan, which should be graded using the rubric

Day 6

1. Students will evaluate contributions of their team members. This should be done during class time, without talking.
2. Ensure that group members are not seated next to one another. Distribute group evaluation forms and read over them with the class.
   1. Each team member should be scored for each category on a scale of -1 to 3.
   2. The TOTAL score for each team member must be different (not 2 students can receive the same score from one student)
3. Have students complete the group evaluations and collect. Use to adjust the groups grade (ie, a team member with very high scores will get a higher grade than the project score and a team member with a very low score would get a lower grade than the project score).

**Lesson Extension: environmental causes of depression**

**Problem Statement: (15 minutes)**

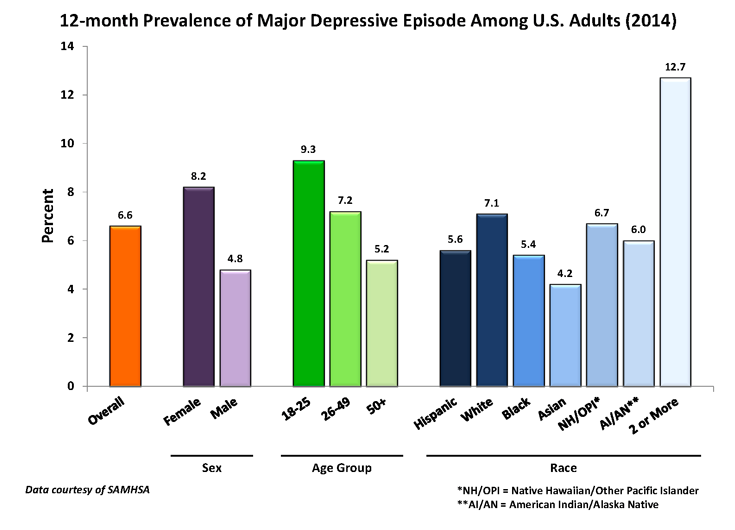
Depression is one of the most common mental disorders in the United States. According to the World Health Organization (WHO; 2010), major depression also carries the heaviest burden of disability among mental and behavioral disorders. Specifically, major depression accounts for:

* [3.7% of all U.S. disability-adjusted life years](http://www.nimh.nih.gov/health/statistics/disability/us-dalys-contributed-by-mental-and-behavioral-disorders.shtml); and,
* [8.3% of all U.S. years lived with disability](http://www.nimh.nih.gov/health/statistics/disability/us-ylds-contributed-by-mental-and-behavioral-disorders.shtml).

The 12-month prevalence data for major depressive episode presented here are from the [National Survey on Drug Use and Health](http://www.samhsa.gov/data/sites/default/files/NSDUH-FRR1-2014/NSDUH-FRR1-2014.htm)  (NSDUH). Based mainly on the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV), in the NSDUH study a major depressive episode is defined as:

* A period of two weeks or longer during which there is either depressed mood or loss of interest or pleasure, and at least four other symptoms that reflect a change in functioning, such as problems with sleep, eating, energy, concentration, and self-image.
* Unlike the definition in the DSM-IV, no exclusions were made for a major depressive episode caused by medical illness, bereavement, or substance use disorders.

In 2014, an estimated 15.7 million adults aged 18 or older in the United States. had at least one major depressive episode in the past year. This number represented 6.7% of all U.S. adults.



**Depression background:**

Depression is a common mental disorder, characterized by sadness, loss of interests or pleasure, feelings of guilty or low self-worth, disturbed sleep or appetite, feeling of tiredness, and poor concentration.

Depression can be long-lasting or recurrent, substantially impairing an individual’s ability to function at work or school or cope with daily life. At its most severe, depression can lead to suicide. When mild, people can be treated without medicines but when depression is moderate or severe they may need medication and professional taking treatments.

Depression is a disorder that can be reliably diagnosed and treated by non-specialists as part of primary health care. Specialist care is needed for a small proportion of individuals with complicated depression or those who do not respond to first-line treatment.

**Learning objectives:** To identify different environmental triggers to depression, discuss solution plan to transfer depression to normal or happy mood.

**How to change unhappiness face to happy face?**



**Standards (NGSS, CCSS, CTE):**

What standards (content and practices) are you addressing in this unit/lesson

1. Generate three poster sections:
2. Depression situation poster: collect depression situations and write on the broad
3. Solution poster: collect actionable strategies or solutions to deal with depression
4. Happyness poster: collect happiness momontents students feel and experienced
5. Divide students into three groups, each group focus on one poster topic and discuss for 10 minutes
6. Intergroup activity: after each group completed inner group discussion, they will interview other group members for commons. (5mins)
7. Whole class activity: each group come to the front of class, present and share group poster to whole class; after each group completed the presentation, it will follow with Q&As. (15mins)
8. Instructor will give quick feedback when the groups complete the presentations; then have a mini lecture about association between environmental triggers and depression, and add commons and guidance for depression actional plan. (15mins)

* Students will record different environmental triggers for depression
* Students will classify depression causes for 3-4 main categories
* Students will discuss the solution plans for depression; it is expected to come up at least three action plans to transform depression to better, normal and eventually happy mood

**Materials:**

**three posters, pen, index papers, usb, color pencils, hands outs, slides**

***Grouping of students for instruction:***

Students will be randomly (or by interests) divided into three groups according to the following instruction and subtopics.

Group discussion:

1. Intra-group discussion length: 10 minutes

2. Intergroup discussion: 8 minutes, following 2 minutes Q&As.

3. Every student need ask or give 3 questions/commons.

4. During class presentation, presenter should share with group discussion summary.

|  |  |  |
| --- | --- | --- |
| Discussion topics | Presenting order | Description/notes |
| Depression trigger from family | 1 | Unhappiness  feeling description: |
| Depression trigger from study or work performance | 2 |
| Depression trigger from peers/coworkers | 3 |
| Depression trigger from other aspects | 4 |
| List things to make you feel happy | 5 | Happiness feeling description: |
| Actionable plan for depression | 6 | Actionable plan summary |

**Procedure:**

1. **Send out handouts of “depression story” (see handout sheet as below)**

**Understand The Problem:**

1. Instructor will launch the problem by introducing a depression story with handouts called “Just perfect” (5-6mins)



**“If I can do it, so can you. I believe in you. I believe in recovery.”**

If anyone had told me several years ago that everything would get better, I would have nodded while screaming disbelief inside my head. I thought things simply could not get better, that I'd be forever feel imprisoned in a dark room. While my friends went out, I chose to remain home. When I went to parties, I couldn’t help but think I'd have had a better time on my own. Even when surrounded by others, I felt shut out, as if I were different from everyone else. And when I found myself in intensive care in the hospital, I couldn’t even bring myself to reclaim my life.

### Eating Disorder Rooted in Depression

It took time, but even I (so skeptical) learned to envision a recovery. And I envisioned myself writing about my recovery, helping others even if I wasn’t quite sure if I would recover. I battled my inner demons for more four years. I thought I wanted to be perfect, but it turns out that I never quite knew what that really was.

But I’m a survivor, living proof that if you put your mind to it, you can overcome your struggles. If I can do it, so can you. I believe in you. I believe in recovery.

I was diagnosed with anorexia nervosa in 2009, although the roots of my illness came from a depression long unnoticed. I received therapy for about four years from two different therapists. When I moved to Slovakia last year, I got a new therapist who is very patient and a great listener.

### Her Best Remedy

However, my greatest remedy is writing. My novel, Just Perfect, is based on the difficult times I’ve gone through. It took me more than three years to write, but it was definitely worth it. I wanted my work to inspire and help others by sharing my own struggles. I wanted to persuade people that they are not alone and that they, too, have a life worth fighting for.

Writing also lifted a heavy burden off of my shoulders. Penning my thoughts and battles was vital, as was the incessant help of my family. Because you can’t win this kind of battle on your own, I urge you to find that person to open your heart to. Speaking with my sister helped me tremendously, preventing my chaotic mess of thoughts from piling up and making me feel more miserable. Without family support, I would not have been able to fight as bravely as I did.

I just want to stress that you, too, should not keep it all locked up inside. So if you have anything you want to discuss or need to let go, I hereby offer you my listening ear in case you ever feel the need because I know you are worth fighting for. I'm sure of it. To all the fighters, don’t give up—and don't be afraid to talk to family, friends, or a professional. I know you can do it. Build trust in yourself and make it happen!

Hanne Arts, who lives in Slovakia, wrote her novel, “Just Perfect” (<https://www.createspace.com/4888416>) hoping to help others struggling with depression and eating disorders understand that they are not alone, and that they can overcome their inner demons. “I hope with all of my heart," she says, "that it will help you on your road to recovery.”

**Explore the Problem:**

Gather Information (5-10mins)

Once students complete reading above story, ask the to answer or find out their answers to the following questions.

What is the cause for this girl’s depression? (Hide Answer: Eating disorder)

What kind of feeling she has? (Hide Answer: lonely, reject to social events)

What kind of way help her get out of the depression? (Hide Answer: writing a novel)

Instructor can write down the students response into a blank board or blank poster.

1. From this story, instructor further divide students into 3-4 groups for intra-group and cross-group discussion and ask them to write down discussion summary. (15-20mins)
2. D. Brainstorm of what students know or need to know
3. Question for students: what kind of environmental factors can cause the depression (Provide hints, negative feelings, illness, lost lovers, stress from working place, colleagues competition, or work load etc)

After completed above discussion, instructor will give a mini lecture to summary about the environment causes for depression. (See below) (10mins)

**Shared lecture information**

Environmental causes of depression are concerned with factors that are outside of ourselves. They are not directly related to brain function, inherited traits from parents, medical illnesses, or anything else that may take place within us. Instead, environmental events are those things that happen in the course of our everyday lives. These may include situations such as prolonged stress at home or work, coping with the loss of a loved one, or traumatic events. Sometimes researchers refer to these as sociological or psychosocial factors since they bring together events that happen out in society with the inner workings of a person's mind.

It has long been understood that experiences we have in our lives can affect our state of mind. The relationships we have with others, how we are brought up, losses we have, and crises we encounter all may affect our thoughts, emotions, and behaviors. How we react to these environmental events may influence the development of clinical depression.

*Traumatic Events*

Many times, people who become depressed report that a single traumatic event happened just prior to their becoming depressed. Painful experiences such as the death of a loved one, divorce, a medical illness, or losing everything in a natural disaster may be so impactful as to trigger clinical depression. Events like these take away a sense of control and cause great emotional upheaval. Some traumatic events may cause more distress for one person than for another. For instance, a man who loses his wife to death may be more prone to becoming clinically depressed than a woman who loses her husband. This may be because the loss of a wife can lead to additional losses for a man. He might lose contact with children and other family members. He may also become more emotionally distressed and isolated if he has difficulty reaching out to others. Women who lose their husbands may be more willing to seek out emotional support.

A person's recovery from depression may also be affected by traumatic events. The more stress and difficulty a person experiences, the longer a recovery from depression may take. For example, imagine a depressed woman in an unhappy marriage who finally decides to file for divorce. If the process becomes prolonged with disputes over finances or custody of the children then her recovery from depression could be slowed down greatly. On the other hand, if the same woman perceived the divorce as something positive in her life, perhaps she was leaving an abusive relationship, then she might have a more speedy recovery.

### *Childhood Difficulties*

People who become clinically depressed have generally experienced more severe difficulties in childhood than those who do not become depressed. These difficulties may include sexual or physical abuse, a turbulent upbringing, separation from a parent, or mental illness in a parent. Some researchers believe that a problematic childhood may trigger an early-onset of depression (first episode occurs before age 20). The most significant event that seems to be related to clinical depression is separation from or death of a parent before the age of 11.

It is not clear just how a difficult childhood can result in adult depression, but there are a few theories. One theory suggests that children who experience great unhappiness growing up have a harder time adjusting to changes in their life such as adolescence and the new roles of adulthood. Another theory is that these children may either lack appropriate emotional development or they become emotionally damaged making them vulnerable to developing depression. Experiencing great difficulties as children, these individuals may be more likely to have low self-esteem, feel powerless, and become dependent on others to make them feel good about themselves. These kinds of traits may increase a person's susceptibility to depression. Still another theory has to do with the developing brain of a young child. Early experiences may affect the development of the limbic system in the brain. If a child experiences great emotional distress, this could affect his or her ability to adapt to new environments and regulate emotions.

During World War II there were a number of children who were separated from their mothers. It was noticed that these children became depressed after going through several stages of grief. First, the children cried strenuously for their mothers. Then the children became very agitated. Afterwards, they became despondent and still. Lastly, they became very withdrawn. This severe reaction to losing their mothers is known as anaclitic depression. This same type of reaction to separation has been observed in studies with monkeys. In these studies, the monkeys secreted higher amounts of cortisol (a stress hormone) during the earlier stages of grief. It was found that the more cortisol that was released into the blood, the more intense the monkey's depression became later on. In approximately one-half of all depressed humans there are high levels of cortisol in the blood.

**Generate possible solutions**

Gathering students actional plan and discuss how to apply it into different depression situation, apply inter and intra group discussion format.

**Resolve the problem:**

Determine suitable solution: Organize class students activities to create depression clinic and let students to mimic doctors to help and consultant the patients for the solutions.

**Present the Solution**

1. Students present solution
2. The instructor will share the solutions (give students hints, such as: exercises, pour out inner feelings, habits, attend parties, take vocation, do something for fun, etc)

**Assessment:**

Assessment criteria: Total points (10) Individual students will be assessed by their group discussion involvement (2), presentation (3), and # of questions they asked (2), # of commons they proposed (2) to their own group and other group, and respect and follow the class role (1); Group will be assessed by all individuals participation, final presentation and group summary reports.

1. Students present solution
2. The instructor will share the solutions (give students hints, such as: exercises, pour out inner feelings, habits, attend parties, take vocation, do something for fun, etc)

**Rubrics**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Student name | group discussion (2 points) | presentation (3 points) | #question/commons asked (2) | respect in class (1) | Total points |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

**Accommodations:**

If there are special student needs, such as visual or physical impairments, instructor need give extra attention and support. When special need students grouped, instructor should communicate with the student, take their request for consideration and place them into a comfortable learning environment. In addition, it is better to send a special instruction to their group member, including the details for how to work with this students during group activities, extra support need be given and set respect standard among group members.

**Extensions:**

If extra time allows, the following activities can be taken into consideration, such as: poster sharing/ picture sharing/ story telling/ watching movies and videos for class discussion

**References/Resources:**

Handouts-- Just perfect <http://www.adaa.org/living-with-anxiety/personal-stories/just-perfect>

Video: Mindmasters: [**https://www.youtube.com/watch**?v=VFrp9ROB44c](https://www.youtube.com/watch?v=VFrp9ROB44c)

10 biggest depression triggers- and how to turn them off <https://www.caring.com/articles/10-depression-triggers?page=2>

The amazing power of your mind: <https://www.youtube.com/watch?v=cLqjK3ddSy0>