Dissecting Huntington's Disease: Introducing Primary Literature Analysis and Collaborative Work via a Gross Anatomy and Histology Laboratory Associated with a Drosophila Inquiry-based Module

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Abstract

In many introductory Biology laboratory courses, students are asked to perform dissections. Often these dissections are assigned with limited contextual information and are assigned as independent assignments disparate from other laboratories required for the course. Over the course of the last several years, the curriculum of the introductory biology laboratory course series at Brandeis University has been completely rewritten to incorporate only inquiry- or project-based protocols with biomedical relevance. As the number and intensity of inquiry-based laboratories has increased, so has the need for proficiency in scientific-literature skills. However, this new curriculum has also reduced the time allotted for traditional dissections. We have designed a one-day dissection and histology laboratory to be performed concurrently with a multi-week Huntington's fly experiment. The Huntington's module incorporated into the spring semester asks students to analyze the effectiveness of a potential inhibitor of Huntington's disease in Drosophila expressing polyQ repeats. During this lab, students dissect a sheep brain taking careful note of structures and features of the brain associated with Huntington's disease progression. Additionally, students perform a Nissl stain on rat brain sections to more closely analyze the distinct composition of the associated tissues. In small groups, the students are then asked to complete an assignment in which they analyze a series of figures taken from primary literature articles related to neurodegenerative diseases. Preliminary results indicated that students found the assignment engaging, relevant to their ongoing Huntington's project, and increased their overall understanding of the use of model systems when studying neurodegenerative diseases.

Brandeis Introductory Biology

- Two-semester course taken sophomore year required for all life science students
- 250-275 students per semester enroll in the course
- Fall: Molecular and Cellular Biology and Spring: Genetics and Genomics
- All laboratory modules are inquiry-based and engage students with a medically relevant experiment series

Representative images of wing morphologies observed on Day 12 of Drosophila expressing Q48. Polymer used in these experiments was an average 10 units long with $\chi_{Tryptophan}$=0.5, $\chi_{Arginine}$=0.1, and χ_{diol}=0.4 ligands. Treatments from left to right are as follows (1) no treatment, (2) 0.5% Polymer, (3) 0.5% Polymer, 10uM Congo red, and (4) 0.5% Polymer, 2.5mM Congo red.

Lab Module: Investigating Huntington's Disease Using *Drosophila melanogaster*

Analysis of a potential inhibitor or enhancer of huntingtin aggregation in PolyQ flies

- Inquiry-based design
- Groups of 4 research PolyQ chemical association and
- Teams select potential inhibitor, concentration and mechanism of delivery to PolyQ Drosophila (Q22, Q48, and Q108)
- Students determine behavioral affects and mortality rates of flies in response to inhibitor

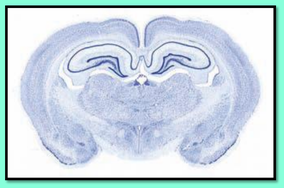
Purpose of the Laboratory and Activity

- Introduce dissection techniques
- Introduce histological staining techniques
- Introduce relevant primary literature to the class
- Increase scientific literacy and data analysis skills
- Encourage cooperation and teamwork in the laboratory
- Demonstrate importance of dissection and observation in analysis of neurodegenerative disease

What are the Elements of the Laboratory?

1. **Dissection of a sheep brain**
   - Inspection and labelling of outer portion
   - Dissection, observation, and inspection of inner areas
   - Connection of inner regions to Huntington's Disease

2. **Histological staining of rat brain**
   - Nissl stain rat brain tissue
   - Visual inspection of features
   - Connection of features to neurodegenerative disease
   - Students work as a class



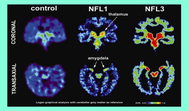
1. **Mouse brain atlas**
   - Visual inspection of sections

2. **Analysis of brain structures and functions**
   - Open Colleges "Interactive Brain"
   - Labelling and connection to disease

3. **Primary literature and data analysis assignment**

Elements of the Assessment Activity

1. **Labelling and identification of parts of a sheep brain**
   - Inspection and labelling of outer portion
   - Dissection, observation, and inspection of inner areas
   - Connection of inner regions to Huntington's Disease
2. **Primary literature I: Chronic traumatic encephalopathy (CTE)**
   - Small, et al. (2013) *Am. J. Geriatric Psychiatry* **2**: 138-144.
   - Areas of the brain affected
   - PET scan data
   - Molecular connection to HD
3. **Primary literature II: Mouse models of Huntington's disease**
   - Wang, et al. (2012) *Nature Medicine* **18**: 153-158.
   - Protective role of Sirt1 in HD
   - Behavioral and molecular assays for HD
   - Statistical significance of data



Outcomes of the Laboratory and Activity

147 students completed a post-test about the assignment

- 75.5% of students enjoyed the dissection while 35.5% indicated they enjoyed the histology portion of the lab
- 90.5% indicated that they would do a dissection again while 57.1% indicated that they would do a histological stain again

Students were asked to explain how the fly experiment and dissection were connected

- Huntington's disease and the areas of the brain it affects
- Genetics and gene analysis
- The value of model organisms
- Generic brain structure and function

Students were asked for suggestions as to how to improve the lab

- Dissect more animals or the current animal in a more extensive way
- Allow each group to do their own staining
- Make the assignment shorter
- Connect the assignment more closely with the dissection

Acknowledgements

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