Max J. Pensack

Personal Information

Address:	150 Claremont Avenue, Apt. 5B, New York, NY, 10027
Contact:	(970) 846-8425 | mjp2143@cumc.columbia.edu
Place and Date of Birth:	Denver, Colorado | July 31st, 1989

Education

Aug 2018 - Present	**Columbia University**, New York, NY Neurobiology and Behavior Ph.D. Candidate - PI: Daniel Salzman
Aug 2016 - Present	**Columbia University**, New York, NY College of Physicians and Surgeons M.D. Candidate, USMLE Step 1: 243
Aug 2014 - May 2016	**Columbia University**, New York, NY Postbaccalaureate Premedical Program Gpa: 3.7030
Aug 2007 - may 2011	**Columbia University**, New York, NY Bachelor of Arts, Philosophy Gpa: 3.5998
Aug 2002 - May 2007	**Steamboat Springs High School**, Steamboat Springs, CO High School Diploma, Valedictorian Gpa: 4.382

Honors and Awards

Summer 2017	Mitsui USA Research Fellowship, Weatherhead East Asian Institute
Summer 2017	IFAP Global Health Research Fellowship, Columbia University
Fall 2015	Harry G. DeMeo, M.D. Scholarship, Columbia University
2009-2011, 2014-2015	Columbia University Dean's List
Fall 2010	William B. & Allan Taylor DeVoe Scholarship, Columbia University
May 2007	Steamboat Springs High School Valedictorian

Skills

Languages:	Japanese (Conversational), German (Intermediate), French & Spanish (Basic)
Coding:	Matlab, R, Python, LaTeX

Research Experience

Jun 2017-
Aug 2017

Research Assistant (volunteer)
Isa Physiology and Neurobiology Laboratory
Kyoto University, Kyoto, Japan

In the summer following my first year in medical school, I traveled to Japan to complete an 8-week rotation in Dr. Tadashi Isa's neurobiology lab. There I had my first opportunity to do experimental work with nonhuman primates. I was involved in two complementary projects - a behavioral project using a visually guided saccade task and a histological project preparing and examining fixed brain slices.

The lab was working to uncover the neural circuits that mediate a phenomenon called "blindsight" in macaque monkeys. Blindsight was discovered in the 1970's in D.B., an epileptic patient who underwent neurosurgery to unilaterally remove portions of his occipital lobe. This effectively lesioned his V1 primary visual cortex, rendering him blind in the contralesional half of his visual field in both eyes. However, he was found paradoxically to have retained some target-finding abilities when presented with stimuli in his visual scotoma. Further investigation into this phenomenon revealed several secondary pathways from the retina that bypass V1 processing. Visual information traveling in these pathways is thought to give rise to physiological and behavioral effects, without leading to the kind of conscious awareness usually associated with seeing.

One of these auxiliary pathways is known as the retinotectal pathway, and carries information from the retina to the pulvinar (Pul) nucleus of the thalamus, by way of the superior colliculus (SC). Another is known as the geniculo-extrastriate pathway, which carries retinal information to the koniocellular layer of the lateral geniculate nucleus (LGN), before traveling on to higher cortical areas. Our research over the summer was focused on performing a double-dissociation experiment to determine which of these two pathways was necessary in the performance of target-finding behavior in V1 lesioned animals. Using muscimol, a $GABA_A$ agonist, we were able to alternatively inhibit Pul and LGN, and assess our animal's ability to accurately perform saccades to targets displayed on a computer screen. We found significant inhibition of target-finding behavior with injections into Pul, lending evidence to the importance of the retinotectal pathway. However, we also observed some mild target-finding inhibition following injections into LGN, but we could not be sure whether the weaker LGN response was due to underlying neural connectivity, or whether we needed to further refine our experimental techniques.

The histological work involved preparing and examining brain slices from a prior V1 lesioned animal. Before being sacrificed, this animal received injections into the SC with an anterograde adeno-associated viral vector expressing the marker dsRed. Working from previous descriptions of SC connectivity in the literature, I examined the slides for evidence of any novel neuroplastic changes that might have occurred in response to the V1 lesion. Although this study only concerned a single subject, the staining appeared to show novel connections from the SC to the lateral and medial aspects of Pul, where previous descriptions had only emphasized connections to the inferior Pul. This work represented a potential anatomical explanation for the retinotectal mediated target-finding activity.

Following the completion of my rotation, I summarized my work in a 45 minute presentation that I gave to members of the lab, and I presented my findings in a poster conference at the IFAP Global Health Symposium on my return to Columbia.

JAN 2016-
AUG 2016

Research Assistant (PAID)

Knight Biophysics Laboratory
The Rockefeller University, New York, NY

I worked closely with Prof. Lawrence Sirovich in his lab at The Rockefeller University, where we tried to develop new computational tools for disease prediction using genome-wide association study (GWAS) data. Specifically, we abandoned the standard method of searching for disease-associated loci, which identifies locations with the highest odds-ratio, and instead used an information-theoretical approach. We showed that the odds-ratio approach is biased toward alleles that are very rare, but are comparatively less rare in disease versus control cohorts. Information-theory provides a way to perform a least-biased sampling of potentially relevant loci, which avoids the pitfalls associated with using an odds-ratio. We applied our methods to the Fusion Study database, which contained 919 genomic sequences from patients with type-2 diabetes (T2D), together with 787 control sequences. We chose this population, because we assumed diabetes to have a strong genetic component, without clear Mendelian inheritance properties.

To perform the analysis, we first split the dataset into two groups, a test and a training set, with roughly equal ratios of cases to controls. Using the training set, we were able to compute the informational complexity associated with each location sampled on the genechip. We then set a cutoff value to select the most informationally salient loci, which differentiated the case patients from the controls. In our final analysis, this step isolated 499 alleles. Using these locations, we were then able to construct a "disease classifier", which was simply a vector containing the loci in question together with the disease-associated nucleobase found at each loci. This classifier is best conceptualized as a string of 499 symbols, each of which has a genomic "address" that points to the most important locations on the genechip. Using these addresses, we were then able to build similar strings for each subject in the test set, by assembling the symbols found at each address. Finally, we predicted which members of the test set were cases or controls based on how well each subject's string matched the classifier. Patients whose string most closely matched the classifier string were assumed to have the disease, while patients whose strings differed were assumed to be controls. Using this method, we were able to correctly predict the disease status of the test set at a rate of 75%. While this was a significant result by itself, the loci associated with the disease classifier unfortunately did not identify any genes that might play a mechanistic role in T2D pathogenesis. However, another exciting application of this approach was that the entire process could be performed in reverse, to create a "control classifier" based on loci that might proffer a protective benefit against the disease in question. Such tools might prove to be useful in researching other weakly-inheritable diseases. Dr. Sirovich published a paper outlining this approach in which he recognized my contributions in the acknowledgments section.

Oct 2014-
Dec 2015

Research Assistant (volunteer)
Brain & Mind Research Institute
Weill Cornell Medical College, New York, NY

At the start of my postbac premed program, I started volunteering with Dr. Gang Wang, an electrophysiologist in Dr. Costantino Iadecola's laboratory at Weill Cornell. There I was first exposed to a variety of basic techniques essential in neurobiology research, such as patch-clamp and field potential recordings, immunocytochemistry, fluorescence microscopy, electrophoresis procedures, calcium imaging, genotyping, and the care and handling of laboratory mice.

I was involved in several projects, the most significant of which was focused on the relationship between Alzheimer's disease (AD) and homeostatic regulation of body weight. Increased body weight is a known risk factor for developing AD, and accelerated loss of body weight often precedes clinically observable cognitive changes in AD. One of the predominant theories of AD etiology focuses on the extracellular accumulation of amyloid beta ($A\beta$) proteins, which are thought to lead to neuronal dysregulation. Previously, the lab had demonstrated that GFP-labeled neuropeptide Y (NPY) neurons in the arcuate (Arc) nucleus of the hypothalamus exhibited abnormal electrophysiological responses in mice overexpressing amyloid precursor protein (APP) or in wild-type (WT) brain slices treated with $A\beta$1-42. To understand what cellular mechanisms might be mediating these changes, we measured membrane potentials and voltage-gated Ca^{2+} influx. In WT mice, we found that leptin both decreased cytosolic-free Ca^{2+} and had a hyperpolarizing effect on Arc NPY neurons in vitro, which was consistent with prior knowledge. Next, treatment with $A\beta$1-42 was found to depolarize those same cells in a dose-dependent manner. We also found that the depolarizing effect of $A\beta$1-42 was reversed in the setting of nimodipine, an L-type Ca^{2+} channel blocker. Lastly, nimodipine restored the resting membrane potential in APP mice to that of WT mice. Together, these findings posited a mechanistic explanation of leptin insensitivity in Arc NPY neurons in the setting of AD. We submitted these results as an abstract to the 2015 Society For Neuroscience conference.

Oct 2014-
Dec 2015

Research Assistant (paid)
Alzheimer's Disease & Memory Disorders Program
Weill Cornell Medical College, New York, NY

At the start of my postbac premed program, I also started volunteering with Dr. Alon Seifan, a neurologist at Weill Cornell who specialized in Alzheimer's disease (AD). I had both clinical and research responsibilities during my time there. My clinical responsibilities included taking vitals, administering neuropsychological exams, and helping to manage the daily office operations. On the research side, I helped to write IRB applications, create and manage the clinical database, and analyze data using R.

Our research efforts were based on a "comparative effectiveness" approach to disease prevention, which represents a potentially powerful alternative to standard hypothesis-based research. Essentially, this project focused on generating a comprehensive online database which recorded patients' baseline health indices, their genetic status, and all prospective medical and lifestyle interventions they might undertake as part of their routine care in the clinic. After all this data was collected, we hoped to work with a team of bio-statisticians to analyze the database and discover what factors proved to have the highest association with preventing AD progression.

FALL 2009 | Research Assistant (PAID)
Hood Visual Science Lab
Columbia University, New York, NY

As an undergraduate student, I spent one semester working in Prof. Donald Hood's visual science laboratory in the Psychology Department at Columbia University. There I focused on a project in MATLAB that used optical coherence tomography (OCT) data to computationally define the boundaries between layers of the retina. This work was later used in a variety of related projects in the lab, which relied on OCT data to characterize the layer-specific changes in a variety of disease processes, such as glaucoma, retinitis pigmentosa, and age-related macular degeneration.

ABSTRACTS

SEP 2015 | *Clinical Trials on Alzheimer's Disease*

Seifan A, Krikorian R, Pensack M, Chen J, Meléndez-Cabrero J, Isaacson R. "A new clinical diagnostic framework for assessing preclinical Alzheimer's Disease in healthy at-risk adults: a work in progress"

SEP 2015 | *Clinical Trials on Alzheimer's Disease*

Haddox C, Gaglio C, Chen J, Pensack M, Seifan A, Isaacson R. "Using social media to educate about clinical trails on Alzheimer's prevention & treatment via Alzheimer's Universe (www.AlzU.org)"

SEP 2015 | *Journal of Prevention of Alzheimer's Disease*

Cooper V, Haddox C, Chen J, Pensack M, Gaglio C, Seifan A, Isaacson R. Multicultural differences toward Alzheimer's education and clinical trial participation on Alzheimer's Universe (www.AlzU.org)"

MAY 2015 | *Society for Neuroscience*

Wang G, Ishii M, McGuire M, Pensack M, Anrather J, Iadecola C. "Voltage-gated Ca^{2+} influx plays a role in Aβ1-42-induced depolarization of hypothalamic arcuate NPY neurons"

WORK EXPERIENCE

2012–2014 | English Teacher
Japan Exchange and Teaching Program
Kumamoto Prefecture, Japan

Worked as a civil servant, assisting with English-language education in the small town of Misato-machi, teaching in two elementary schools, one junior high school, and an adult education class.

2006–PRESENT | Tutor

Freelance tutoring experience with elementary school through college age students. Subjects include SAT/ACT preparation, math, science, and writing.