Multiple sclerosis (MS) is a chronic immune-mediated disease characterized by inflammatory demyelination and progressive neurodegeneration, resulting in the primary non-traumatic cause of disability among younger adults. The disease is thought to be triggered in genetically susceptible individuals by a combination of one or more environmental factors; however the exact cause of the disease is currently unknown. When the disease flares up it imposes a tremendous impact on patients’ personal lives because the course of its progression is unpredictable and may vary among 4 different types: relapsing-remitting MS (RRMS), primary-progressive MS (PPMS), secondary-progressive MS (SPMS), and progressive-relapsing MS. Most of the currently available MS drugs have proven to be effective only against RRMS, leaving an important unmet need for patients with progressive forms of MS.

New data presented at the 2015 Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) have changed this therapeutic perspective. Results from three phase III trials of a new therapeutic agent, Ocrelizumab (Roche/Genentech), a humanized monoclonal antibody that depletes CD20+ B cells, have proven impressive efficacy for the treatment of both RRMS and PPMS. Ocrelizumab becomes the first investigational medicine to show efficacy in people with primary progressive forms of MS, and was shown to result in the reduced risk of confirmed disability progression. Moreover, Ocrelizumab also significantly reduced lesion volumes and brain volume loss of patients. Importantly, all three trials demonstrate the safety of Ocrelizumab. Over two years of treatment, Ocrelizumab significantly reduced the relapse rate (~47%), the risk of confirmed disability progression by 40%, and the number of inflammatory lesions (95% reduction) when compared to IFN-β1a.

After completing its pivotal trial program, Roche/Genentech now anticipates filing Ocrelizumab for approval in early 2016, meaning potential commercial availability in 2016 or 2017. All together these results were described as “ground-breaking” and “game-changing” by key opinion leaders of the field and will introduce a new benchmark for the treatment of both RRMS and PPMS.

REFERENCES:

The Sequence Lives of Neurons

By Andrew Koemeter-Cox

Cells in the human body accumulate mutations over the life of their host due to a variety of mechanisms. Until recently, genome sequencing required the isolation of large amounts of DNA from tissues, which would obfuscate the unique mutations present in individual cells. Single neurons in the human brain have decades to accumulate mutations, which two laboratories at Harvard University have recently characterized (Science 2 October 2015).

The groups employed single-cell sequencing to examine single-nucleotide variations (SNVs) in 36 neurons from the post-mortem cerebral cortex of three individuals. SNVs unique to the genome of individual neurons were identified by comparing them to sequenced DNA from tissue samples from the respective subjects. Analyzing the sequencing data using a number of algorithms and statistical tools, the authors determined that each neuron contained around 1500 unique SNVs.

The unique neuronal SNVs were more likely to be located in transcriptionally active regions of the genome, differing from SNVs in cancer cells, which are commonly found in late replicating DNA. Mutations shared among an individual's neurons revealed developmentally-related cells. Closely related neurons could be spatially distant, indicating that cells from different progenitors are interspersed across the brain. Interestingly, some neurons, SNV-wise, were found to be more closely related to cardiac cells than nearby neurons.

This fascinating work reveals that each of the over 100 billion neurons in the brain of a human being may have its own unique set of mutations. The genomic distribution of these mutations reveals that highly transcribed genes are the most susceptible to damage over the long life of the neuron. Analysis of SNVs that are unique and shared among cells allows their lineages to be traced, and may eventually assist in providing a highly detailed map of human brain development.

Co-Chair Corner

Greetings fellow postdocs,
Ahh yes, ‘winter is coming’…and with it a new year! So in addition to all of your new year’s resolutions, why not set up a LinkedIn account and start planning for your next career move? The hiring season is upon us and now is the perfect time to get your résumé and curriculum vitae up to date, expand your social network, and land that dream job!

The Postdoc Executive Committee (PEC) would also like to send out a few ‘high-fives’ and ‘job well done’ handshakes to former Co-chair Merina Varghese. If you see her walking around Mount Sinai please be sure to say ‘thank you’ as she has done a fantastic job leading the PEC, organizing the 6th Annual Postdoc Symposium, and advocating for postdocs’ needs especially through her work with the new Code of Conduct for Postdoctoral Trainees and their Mentor(s) agreement. Best of luck to you, Merina, as you transition into the next stage of your career! Without further ado, let me introduce Alison P. Sanders as the new PEC Co-chair!

Finally, please join us next Friday, December 18th from 5-7pm for our last Postdoc Social of 2015!

Best,

Alison P. Sanders and Ryan J. Cummings are your PEC Co-chairs.

Ways to keep in touch
- Our website: http://icahn.mssm.edu/education/postdoctoral-training
- Follow our Twitter account: @MtSinaiPostdocs
- Join our Facebook page: “Mount Sinai Postdocs”
- Follow us on LinkedIn (Mount Sinai Postdocs and Postdoc Alumni)

The Mount Sinai Postdoc Periodical
Chief editor: Delaine Ceholski Editors: Przemek Gorski, Alaa Abdine, Octavia Bane, Mar Gacias-Monserrat, Natasha Eliyahu-Shtraizont, Olivia Engmann, Andrew Koemeter-Cox, Laura Lecce, Chiara Mariottini, Salvador Sierra
We navigate our lives through a framework of assumptions. Optical, auditory and tactile illusions show us how easily our sensory faculties can be deceived. We have never seen planet Earth from space with our own eyes and yet we trust that it is spherical. We did not evolve to be the ultimate critics. We try to make sense of the world by generalizing, stereotyping and overemphasizing relevant exceptions. But what about facts we know to be false? Take, for instance, Santa Claus. Most of us grew up with a neighbor or uncle showing up at Christmas, wearing a beard and red coat. In my case, along with my Dad and sister, we would peek through a keyhole and watch my Mom offer Santa a Schnapps or two in exchange for our gifts, having a drink herself, while chitchatting flirtatiously. It seemed a plausible story at the time. Naturally I know better now.

A recent publication by Fazio et al. in the Journal of Experimental Psychology suggests why knowledge may not prevent us from illusory beliefs: The researchers show that despite knowledge of a given fact, such as “The Pacific is the world’s largest ocean”, repetition of false facts can result in a faulty belief (“The Atlantic is the world’s biggest ocean”), even when it is emphasized that the new facts are false. The Illusory Truth Effect is backed up by a large pool of research that points in the same direction: The fragility of our belief system. For instance, facts written in high-contrast fonts are perceived as truer than facts in low-contrast fonts (Reber & Schwartz, 1999). It is similarly easy to have a person state a false fact by the way a question is asked – an effect called the Moses Illusion (“How many animals did Moses bring to the ark?” Answer: “Moses brought two of each animal to the ark”, even though the participants had learned that Noah had only built the ark and were warned about faulty questions). Taken together, it is evident that our beliefs are shaped by repeated exposure to facts that are not necessarily true – we can even know that they are false. Whether this is Santa or a presidential candidate in the media that we perceive as outrageously unreasonable – they will inevitably affect our future beliefs. Moreover, we typically forget our source of knowledge and what persists is the belief itself, true or not. Our brains evolved in order to extinguish old knowledge when new knowledge is repetitively presented. This can result not only in superstition but also in implicit bias.

This Christmas, let’s make a gift to ourselves and others by avoiding the exposure to unreasonable media statements. Instead, let’s observe why we hold certain beliefs. Let’s remember that Santa Claus was an old man from Scandinavia and the three gift-bearing Kings at Jesus’ birth were ethnic minorities, likely without a national work permit. Let’s judge them for their actions, not their backgrounds.

---

UPCOMING EVENTS

- The Office of Career Services and Strategy Winter sessions are in full gear! Check out “NEW JOB’ Negotiations (Presentation/Discussion)” on December 16th from 4-5 pm in CSM 5-101 (bring questions!). Please email ellie.schmelzer@mssm.edu if you have any questions about these seminars or if you would like to schedule a meeting to discuss your future career plans!

- Writing seminar: The next seminar is January 12 at 4pm. Stay tuned!

- The Postdoc Writing Group meets the 3rd Friday of each month at noon in Hess Center room 10-122 (10th floor). The next meeting is December 18. If you have writing to work on, bring a few copies of it (1-2 pages, ideally an abstract or introduction and no results or methods sections). The group will also read CVs and cover letters. Follow the ISMMS Postdoc Writing group on twitter @PostdocWriting. To join the mailing list visit: http://mailman.mssm.edu/mailman/listinfo/postdoc-writing

- Next Postdoc Social is Friday, December 18 at 5pm in the Icahn MC Alcove. Come for food and drinks!
The Bullsh*t Factor: Acceptance of Profound-Sounding Phrases Linked to Lower Intelligence
By Delaine Ceholski

While bullsh*t is common and has been recognized by philosophers (and basically everyone else) for years, it has never been studied empirically. This task was taken on by a group at the University of Waterloo in Canada, who used “seemingly impressive assertions that were presented as true and meaningful but are actually vacuous”\(^1\) to test how amenable people were to bullsh*t. These profound statements were computer-generated to be completely meaningless, but use organized linguistic structure so that they appear to communicate something (e.g. “Hidden meaning transforms unparalleled abstract beauty”). Three hundred participants were asked to rank the randomly-generated bullsh*t phrases on an arbitrary scale of 1 to 5 (mundane to profound). A frightening twenty-seven percent of participants ranked the phrases as profound to very profound. Next, the researchers used real-life examples of bullsh*t phrases - more specifically, they used phrases from Deepak Chopra's Twitter feed\(^2\). They found that the ranking of these phrases by the participants was similar to their ranking of the computer-generated ones, indicating no inherent differences between real and fake bullsh*t.

The numeracy skills, verbal intelligence, religiosity, and ability to differentiate between a metaphorical and literal statement were determined for each participant. The authors concluded that the participants more likely to rank bullsh*t statements as profound were of lower intelligence and were more likely to believe in conspiracy theories, the paranormal, and alternative medicine. Published in the Journal of Judgment and Decision Making, this paper used the word “bullsh*t” over 200 times (that's got to be some sort of record) and even establishes its own Bullsh*t Receptivity Scale, termed the BSR. While it's easy to dismiss the paper solely on its repetitive use of the word “bullsh*t”, the authors end on an introspective note: “One benefit of gaining a better understanding of how we reject other’s bullsh*t is that it may teach us to be more cognizant of our own bullsh*t”. While the paper may not be profound, it is indeed meaningful.

REFERENCES

2. Deepak Chopra Twitter Feed. URL: https://twitter.com/DeepakChopra.

Happy Holidays From The Postdoc Periodical Team!