

July 6, 2020 newsletter.

Dear Grey House team and esteemed colleagues,

125 days into our protracted team-building adventure, and in the immortal words of the Grateful Dead, what a long strange trip it's been. In the past 14 days New Zealand had 21 cases, Norway had 203, Demark 441, Israel had 7,716, the UK had 12,187, and Sweden had 15,276, as compared to 26,117 for North Carolina (pop 10.5 million).

Top holiday picks with 0 cases reported to WHO: Brunei, Falklands, Faroe Islands, Geenland, Grenada, Guernsey, Isle of Man, Laos, New Caledonia, Tanzania. Let's go!

This week's newsletter theme is: Animals, domestic, wild, or otherwise imagined, including penguins. Pics at the end, as always!

Meanwhile, here is the all the news I have that's fit to print since 29 June:

FIRST THE HAPPY NEWS!

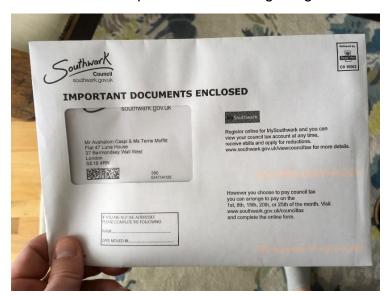
Britain has opened the pubs!



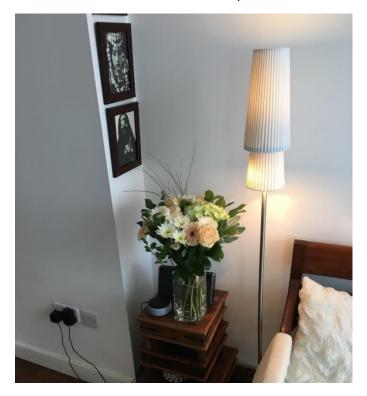
Kyle got the Perceived Stress Index inserted in the Duke module of the Cooperative Congressional Election Study, a 36,500-person national survey of the American electorate, pre and post election. https://cces.gov.harvard.edu/)

25 July: Antony Ambler will celebrate his 20th birthday!

Still locked down in our small flat in Shad Thames, since March (!), Antony is a hero. This is the sort of post he has been getting:



Antony could obviously benefit from your cheery birthday greetings. Our Grey House team did send him a Pesh bouquet this week to start the birthday month.



Line's paper is accepted the Journal of Gerontology: Medical Sciences. Hurrah! Hurrah! "Association between elevated suPAR, a new biomarker of inflammation, and accelerated aging"

Adrienne Romer's paper is out at last! <u>Pervasively Thinner Neocortex as a</u> Transdiagnostic Feature of General Psychopathology

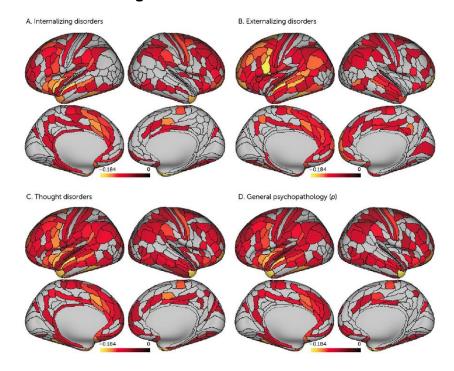
Romer, Elliott, Knodt, Sison, Ireland, Houts, Ramrakha, Poulton, Keenan, Melzer, Moffitt, Caspi, & Hariri (2020). A pervasively thinner neocortex is a trans-diagnostic feature of general psychopathology. <u>American J of Psychiatry.</u> Consistent with the high comorbidity of symptoms and diagnoses, Dunedin data reveal that the underlying brain structural correlates of mental disorders are unlikely to exhibit specificity, suggesting that it may prove more fruitful to pursue common rather than distinct mechanisms of general psychopathology in advancing efforts to improve prevention and intervention.

We have an idea for Leah's send-off party! Leah and Curt leave Durham to start their new lives in Ann Arbor Michigan in August. So one weeknight between 13 July and 31 July, we are hoping to drive our cars to Grey House, park them facing the east side of Erwin Mill (thus in the shade), and have a pizza delivered to each car. Susan is investigating logistics: can we get permission from the property owner, and will Mellow Mushroom Pizza deliver? Stay tuned! And get going writing your limerick or haiku!

NEXT, THE UNHAPPY NEWS: The news from MRC about our E-Risk application is not happy. Jolly good thing Britain opened the pubs! I spoke this morning with program officer Karen Brakspear. The bottom line was that although there were some board members who were real champions for the application, there were others who did not believe the social sciencey questions in our aims warrant the cost of following up a cohort. Karen frankly said, if the grant had been all about genetics and epigenetics and biomarkers, it would have been a better match to this board. Some board members believed that getting blood was the only reason for the face-to-face home visit data collection. They did not buy our argument that cohort retention and clinical mental health data quality are better in home visits than in internet surveys. So, they thought the cost of home visits has got to be explained by lots of primary aims using blood. The Neuroscience board did not get excited enough about the guestions about how childadolescent mental disorder and victimization influence young adults' stress, trust, human capitol building, and social mobility during a severe economic downturn. Unfortunately the ESRC representative was unwell and did not attend. The application is not deeply flawed, it was just a poor match to this board's interests. Our 6 peer reviewers scored the application a mean of 5.5 out of 6. The board scored it a mean of 7 (some 5's, some 9's), and MRC funded all the applications with scores of 8. We came very close. So what's next? We can resubmit to MRC in January with all-new aims about genetics and epigenetics and biomarkers. And/or we can submit to the US NICHD this autumn an application that is closer to this current one, but probably with added aims about genetics and epigenetics and biomarkers. Our inclination at this moment is to do both. Chin up! We will get there together!

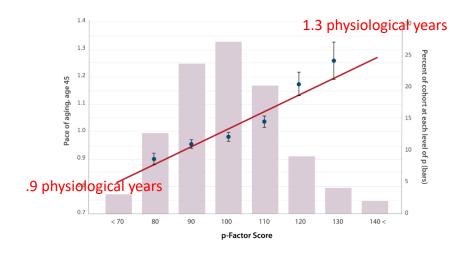
Science-visualizations:

Can you spot the specific thin cortex regions related to different kinds of mental disorders? I thought not.



Romer, Adrienne L. et al. (2020). A pervasively thinner neocortex is a trans-diagnostic feature of general psychopathology. <u>American J of Psychiatry</u>

From Jasmin: Higher p (cumulative history of general psychopathology) is associated with faster pace of aging to age 45, in physiological years per chronological year. R= .21.



RESEARCH-PROJECT PROGRESS SINCE 29 June:

With more than 30 papers in review, delays can feel dispiriting, so I'm only reporting papers here that have made progress this week. Chin up! Patience builds character.

New Concept Paper from Tracy: Microstructural integrity of whole-brain white matter tracts and midlife physical fitness.

From Jasmin: I want to give a shout-out to **HonaLee** for so patiently providing me with new variables for the p-and aging paper in recent weeks! We came up with a lot of additional analyses, which translated into lots of variable requests, and I just thought it would be nice to appreciate her efforts in supplying me with those (in record time, too).

Tracy got an R&R at Geroscience! This is super because it's her major area review paper for the PhD. Cardiovascular fitness and structural brain integrity: An update on current evidence.

Kyle got an R&R at Clinical Psych Science! Hurrah! Lower cardiovascular reactivity is associated with more childhood adversity and poorer midlife health: Replicated findings from the Dunedin and MIDUS cohorts.

Maria Gehred's first-year project paper was submitted to Neuron. "Long-term neural embedding of adverse childhood experiences: a population-representative birth cohort followed for five decades." Good luck Maria!

A heroic effort! Aaron and Max's paper has been revised for resubmission to JAMA. 12 single-spaced pages of revision requests, and revisions completed by the 2-week deadline. The Dunedin age-11 lead-exposure data are the gift that keeps on giving. Association of childhood lead exposure with structural brain integrity in midlife.

Renate this week helped Aaron and Max with complex rapid-response analyses for the revision at JAMA. Thanks heaps!

Tim matthews's revised paper was re-submitted this week: This is what loneliness looks like: a mixed-methods study of loneliness in adolescence and young adulthood" International Journal of Behavioral Development

Jessie Baldwin's paper got transferred from JAMA to JAMA-Pediatrics, and she has been invited to revise it for them. Population versus individual prediction of poor health from Adverse Childhood Experiences (ACEs) screening. Better luck there Jessie!

Max and Avshalom's paper will be submitted to Nature Aging soon: Disparities in the pace of biological aging among midlife adults of the same chronological age: Implications for early frailty risk and policy.

Christina Carlisi and Essi Viding's paper will be submitted soon: Associations between life-course-persistent antisocial behavior and subcortical brain volume in a population-representative longitudinal birth cohort. THANKS TO ALL WHO DID MOCKS!

Tracy's literature review on fitness and the brain is in review at Geroscience.

Projects underway and making good progress on the march toward mock review:

Aaron Reuben and Helen Fisher, air pollution and mental health (E-Risk).

Leah Richmond-Rakerd, Barry Milne, Stephanie D'Souza, mental disorder predicts physical disease and mortality (NZ-IDI)

Jasmin Wertz, Little p psychiatric history and pace of aging (Dunedin)

Leah and Signe Andersen, education disrupts the intergenerational transmission of disadvantage (Danish registers)

Jasmin Wertz, parenting genomics in multiple cohorts (many cohorts)

Kyle Bourassa and Line Rasmussen, stressful life events and suPAR (Dunedin)

Max Elliott & Line Rasmussen brain and suPAR (Dunedin)

Karen Sugden, education and the methylation pace of aging (many cohorts)

Geli Ronald and Lizzie, Autism Q and p (Dunedin)

Franky Happe and David, Autism Q and midlife health (Dunedin)

Tim Matthews in London is writing a proposal to UKRI for a short survey to see how E-Risk twins cope with the 'new normal' after lockdown.

Annchen, Christina Carlisi, and Max resolved this week the thorny question of whether neuroimaging papers should routinely control for total brain volume. NO! NOT AT ALL! This required a lot of literature review, some history delving, data analyses, and several zooms. It's a little complex to explain in a newsletter, but if you want the scoop, just ask.

Aaron submitted a proposal to the NIA Telomere Research Network for a small grant to test whether childhood exposure to lead leaves a signature in Dunedin Study members' telomeres. Idan Shalev and Karen Sugden will help, as will Ben Williams.

Barry and Stephanie in Auckland are doing the final runs in the NZIDI for the new paper with Leah on mental health and physical health.

Ben is creating new polygenic scores: for Jorim Tielbeek's antisocial meta-GWAS in E-risk and Dunedin. He's also deriving the education3 polygenic score in the ALSPAC data that Jasmin has obtained. Thanks Ben!

Ben is further investigating brain biomarker plasma assays, investigating UK data sets that have methylation data for validating the DunedinPoAm, and reviewing methodology for Dunedin and E-Risk telomere work.

Karen, Chloe, and Helen are testing whether DunedinPoAm can be derived from cheekswab DNA, not just blood. This would allow wider export of the technology.

Karen is doing a server clean-up of HARDAC, to make room for incoming megadatasets for our team's polygenic and methylation studies.

Antony Ambler in London is finalizing the data set for family history of dementia, collected by the Dunedin Unit team through phone-call interviews with Study Member's mums. **Variables ready soon!**

Sean Hogan in Dunedin is searching admin register data for Dunedin Study members.

Susan has been processing our finances for end of the fiscal year on 1 July. And also helping Aaron, Leah, and Jasmin with grant materials, working on **Stephanie's visa**, and maintaining our website. www.moffittcaspi.com

Honalee's creating a spreadsheet table of reasons for missing data at Phase 45 in Dunedin. Yes, 94% of Study members took part at 45, and Renate's great attrition analysis figures show these 938 represent the original cohort. However, variable by variable, there are data missing for many reasons: equipment failure, session chronically running overtime and last measure skipped, staff mistakes that crept in after training, Study member reluctant to try a task, lab tissue samples lost or given wrong SM ID number, software glitches, interview booklet pages not printed by the printer, skip patterns incorrect on interview forms and items skipped wrongly, Study member's foot or hand injury precluded a functional test, etc. Before phase 52, we want to inform PI's about opportunities to improve their data-collection and avoid missing data.

Renate's thinking about how to get little p out of the NZ psychiatric hospital and pharma prescription data sets.

Antony Ambler in London is doing the reproducibility stat check for Stephanie's Lewis's paper on trauma.

Annchen, Maria, Max are working on characterizing gradients of brain organization.

Jasmin's working with Sara Jaffee on an application to study the Next Gen sample of Study member's children in Dunedin.

Tracy finished her dissertation proposal and will defend it soon. It is all about physical fitness and the brain.

If you are working on something you want others to know about, but I missed it, please let me know.

This week's theme:

Animals: domestic, pets, wild, or otherwise!

FIRST, OUR DOG FRIENDS:

Candice's daughter Ava and dog Luna watching the fireworks – and socially distancing – from our rooftop this July 4 in California.



Remember Vente who visited Grey House?

Adam Schmidt's lovely dog, from a May newsletter



Annual Jack Russel race, Wanaka Agricultural and Pastoral Show, New Zealand.



From Stephanie in Auckland: My dog Zoe and her best friend Homie, who moved away just before we went into lockdown. He used to escape from his house and come over to ours to play with her at least once a week.



From Leah and Curt: Eli's hiking trip to the Appalachian Mountains.



Susan's Bitsy, who loves working from home. Very helpy!





NOW CATS!

Alice's Bagheera in London.

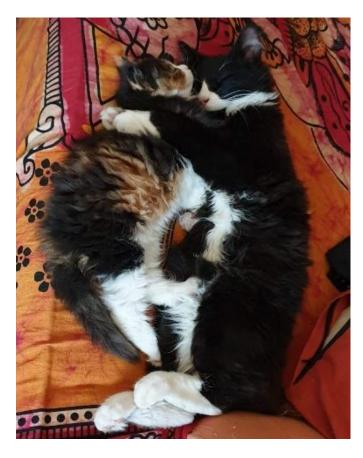


Honalee's cat Squeak likes making data sets for you.

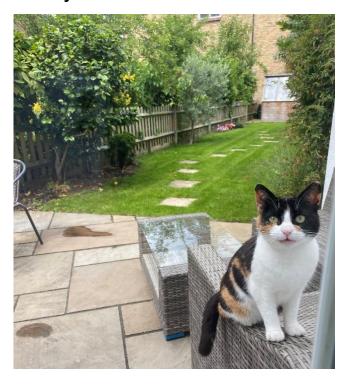


Jo Newbury's cosy puzzle cats in London, Basil and Furby.





Jessie's little neighborhood friend in London, loves to visit, even tho she isn't actually Jessie's cat. How do we know she's a she? Can you guess?



Renate's cat, Autumn, so helpful with yard work. Or is that the old box trick?



FISH?

Kyle's striped bass pet.



REPTILES?

A Madagascar chameleon. Rather an ironic facial expression.



NEXT BIRDS: Jo and Jude's chook, dressed in best jumper in Peterboro, UK.





Helen's swan and cygnets, spotted while kayaking on the Thames in London.



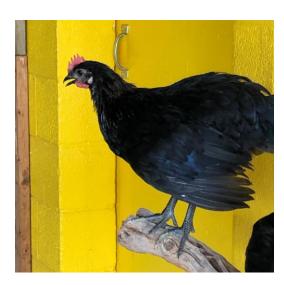
Chicks and ducklings at Tractor Supply.



Turkeys at Temi and Av's farm, getting ready to wife swap, apparently.



Avshalom's friend Poppy Seed on the Macon Farm.





Christina's lovely cygnets in London.

COWS EVEN?

Jenny Van Dongen's June holiday in rural Holland, with Holstein Freisiens.



Their American counterparts, on Temi and Avshalom's farm, 1966.



Their New Zealand counterparts:



WILDER FARE:
Andrea Hussong's birdbath ice-skating squirrel.



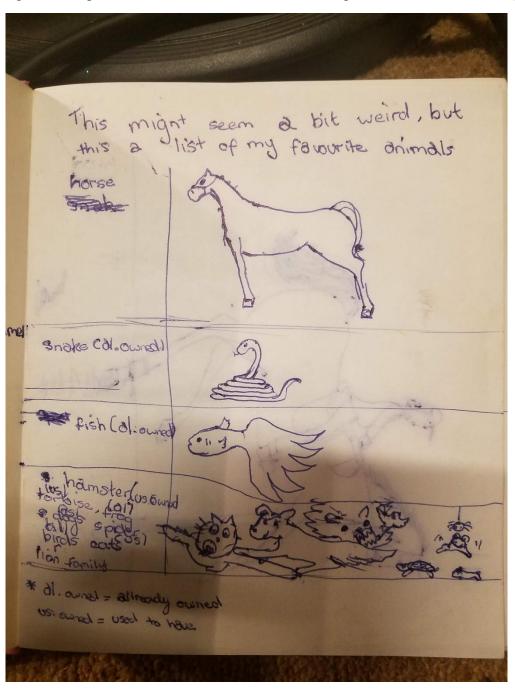
A New Zealand brushtail possum. Sorry, this bloke was caught red handed raiding the garden in St. Bathans.





They do have lovely fur, but make truly horrible sounds.

Horse and snake and fish and hamster? From Karen: I know everyone is probably sick to death of seeing the actual real animals I am hoarding now, but here's a bit of insight to where my penchant for animals comes from....This is a page out of an old diary of mine I found whilst cleaning out my parent's attic last year. I was probably around 9 when I wrote it (I guess?!?). Anyway, a bit of horse obsession from a tender age, although wasn't so aware of snakes coming such a close second 5



Remember Barry's rabbit stalker, from a May newsletter?



Wishing you all a serene week, Temi

