Age-dependent impact of early-life stress on glia and synapses
Substrates for increased risk for Alzheimer's disease
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Appendices
“One must imagine Sisyphus happy”

Albert Camus
Acknowledgments

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First of all, I’d like to thank my promoters. **Aniko**, you took a chance on me all those years ago, first as an intern, and then as Lianne’s successor. It has been a wonderful journey, and I thank you for taking care of me, and investing both in my personal and professional growth. Your optimism and insistence on finding a silver lining is a skill I have yet to fully master, but they have certainly helped during the various challenging moments of the past few years. You showed by example how to do science in a truly collaborative manner, which I hope to embody in everything I do in the future. At the end of the day, you gave me a space to grow, as well as multiple opportunities to have seats at very important tables, and I will be forever grateful for our time together and the many doors you have opened for me.

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I would like to express my gratitude to the members of my doctoral committee, drs. **Bart Eggen**, **Inge Huitinga**, **Frank Jacobs**, **Helmut Kessels**, and **Shane Liddelow**, for taking time out of their busy schedules to evaluate this thesis. I look forward to discussing this book with you.

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**Silvie**, look at how your “favorite student” is now doing! We’ve been through so much together, from perfusing during a snowstorm, to writing CCD “applications” “sober”, as well as weighing a bazillion mice and their consumption. Beyond forming a kick-ass team, I always appreciated how you treated me like family, like that one Christmas we hung out. It was such a joy to sit next to you every day, and I hope that we can recreate those good times again someday. I wish you all the best in your personal and professional journey in Switzerland and beyond. Miss you!

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grounded presence (and a great listener too!), I miss just being able to have coffee with you and talk about the bigger picture things in life. I just wish we had more time to do all these other cool things, but in any case just hope that you are enjoying being back home!

To the current members of the lab, thank you for our time together. I’ve been on and off writing this part during my last few weeks of loitering in the office, and I can’t help but wish we could be colleagues forever. I would take a bullet for you guys (but only in the form of doing last minute animal duties), and sincerely hope that my departure from the lab does not spell my departure from your lives.

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Jen, I don’t even know where to start. Thank you for always being a ball of warmth for everyone in the group, even if sometimes you burn at your own expense. I am thankful for all the wonderful times we’ve shared together. As the only other R nerd in the group (for now), I’ve come to look forward to various technical discussions with you. Beyond that, I truly appreciate how much you care for all of us, and only wish that you also see how much we all care for you as well. Your passion for science is inspiring (and might have even been contagious under different circumstances), so I hope that you take good care of yourself, because I truly want to see how far you will go (trust me, it will be quite far).

Gideon, you are literally one of the people who have been there for me from the start. I thank you for always thinking along with my problems, and for always being willing to answer the stupid (repetitive) questions I ask you, especially when the experiments get big and I start doubting myself too much. Beyond science, I will always cherish our countless coffee breaks, the times we would play video games together, and of course our trip to Brazil. I wish you all the happiness and fulfillment in the world, and hope that you always find the things in life that spark joy.

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Hannah, it has been so nice to see you grow out of your shell. You’re even doing various lab stuff now! I hope you don’t forget to have faith in yourself, no matter how out of left field the things you do become, as you are definitely capable of rising to the occasion. You’re going to be great!

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Wouter, it has been a pleasure to get to know you in the short time that we’ve been in the group together. I wish you all the best with your postdoc!

Xiaoyi, 认识你很高兴。希望你除了每天认真工作也可以好好的享受在荷兰的这几年。你的努力肯定会有好的结果的。祝你实验成功！

I would also like to mention the students I’ve had the privilege to supervise and work with over the years: Henok, Vera, Astrid, Jill, Sophie, Ella, Roberta, and Luca. Thank you for all your hard work and dedication to your projects. Your presence and enthusiasm have been saving graces during my low periods. I look forward to your continued growth as scientists and people, and am assured in knowing that all of you are destined to surpass me in your success in both.

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there! Thank you for our moments of commiseration. All I can say is, we somehow managed. To my Portuguese brother Luis, it has been a privilege to get to know you so well. You are so sincere in all your interactions, and I just appreciate you so much. Take care of yourself, I’m sure you will do great things both in science and also beyond. To my fellow interns-turned-colleagues, Judith and Joost: it seems like just yesterday we would gather at the common area during Friday afternoons for drinks. Thank you for being there from the start. I wish you all the best, and hope to be there at the end of your respective journeys too. My thanks as well to all the other colleagues over the years: Elias, Swip, Elise, Julien, Jean, and Eddy (and a lot more I’m sure I miss, my apologies!). I really enjoyed all the fun borrels, social interactions, and idea sharing we had.

My projects have greatly benefited from the wonderful collaborations that I was fortunate enough to be a part of. To drs. Elly Hol, Marian Joëls, Gijs Kooij, Mark Verheijen, and Elga de Vries, and their respective labs: I really appreciated the new insights and perspectives that you brought to our different projects. Thank you for your generosity in sharing your expertise and knowledge with us, you have all taught me so much.

I would like in particular to thank members of the Eggen lab at the UMCG: Bart, Suus, Laura, Nieske, and Takuya. It was an eye-opening experience to learn from you throughout the various collaborations between our labs. Getting to join your team is like a dream come true, and I look forward to all the cool new projects that we’ll work on together!

I was also fortunate to have made so many friends at a similar career stage these past years. To Christiaan, Isadora, Jelle, Joeri, Mandy, Miao, Rob, Valeria, and others that I am surely missing (sorry!): thank you for the sense of community that you gave during our discussions related to science and life. Whether it be a conference, party, retreat, or a chance meet-up, seeing you guys always made my day, and I look forward to seeing what cool things you will be up to in the future.

My journey to becoming a neuroscientist in Europe would not have been possible without the Erasmus Mundus Neurasmus program, which generously funded my MSc studies. Beyond that, it also provided me with lifelong mentors and friends who have been an integral part of my network here in Europe. In particular, I’d like to thank my Neurasmus family in Amsterdam: Elena, Julia, Kanishk, and Vicky, who I could always count on for non-work related perspectives. I also owe quite a bit to Anna, who recommended the Korosi lab to me based on her previous internship. Shout outs as well to Sahana and Marta, integral parts of our tri-synaptic circus who have remained close to me despite the geographical constraints our chosen paths have placed on our friendship. Thank you all for taking care of me, especially when I was but a kid who moved to Europe to live alone for the first time. During my stay in Neurasmus (specifically in Berlin), I was aided by two incredibly patient supervisors, Özgür and Nutabi, who probably lost so many brain cells teaching a psych grad how to pipette/genotype and do Western blots, respectively. I would not have made it here without your investment in me; thank you.

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for four wonderful years (ball is life!). Coach Guiseppe, I would run into a wall for you. Thank you for making me a better player, and for always pushing and believing in me. To my fellow players (esp. the beginner gang: Athos, Jassine, Jelke, Kingman, Mor, Lev, Quinten, Tristan, Wouter, +++), thank you for the camaraderie and competition. Every week in these past years, I’ve looked forward to getting to play the game we all love on Mondays and Wednesdays. I look forward to our next game.

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To my dad Johnny and my mom Sining, thank you for instilling in me the drive to learn, and for loving me enough to let me enjoy my adventures here, even at the cost of severely reducing the time we can spend together as a family. Only in being forced to be a proper adult in Europe have I realized how much you did for us growing up, to ensure that learning and being kids were the only tasks we had to worry about. I love you, and thank you walking to ensure we could fly.

To my brother Karljan, the soon to be (actual) doctor Kotah: I love you, and I’m so proud of you. When I left, you were just starting your studies, and now here you are, on the verge of becoming a medical doctor, and already saving lives. I’m so sorry to not have been around more during these fun and formative years, and to force you to take on my share of responsibilities at home. May you get to chase your dreams like I did someday, and take a path that rewards you with everything you deserve.
To Yuri, thank you for both your patience in being together long distance, as well as all the adventures that we have shared since you moved to study in the NL. Life here is more fulfilling and rewarding with you around. I hope to be able to support you in the pursuit of your dreams in the same way you have been there for mine. I cannot wait to have more wonderful memories that we will forge together, and I look forward to continue choosing you every day. I love you.

Lastly, and most importantly, none of this work would have been possible without the animals used in these experiments. May at least one thing in this book prove their sacrifice worthwhile.
Appendices

Curriculum Vitae and Portfolio

Education

09/2022 – present: Postdoctoral researcher, University Medical Center Groningen, NL, with prof. dr. Bart Eggen and dr. Susanne Kooistra

10/2017 – 07/2022: PhD candidate, University of Amsterdam, NL, with dr. Aniko Korosi and prof. dr. Paul Lucassen

09/2016 – 08/2017: MSc (Res) Neurosciences, cum laude, Vrije Universiteit Amsterdam, NL (under Neurasmus Joint Masters program)

10/2015 – 08/2016: MSc Medical Neurosciences, Charité Universitätmedizin Berlin, DE (under Neurasmus Joint Masters program)

06/2011 - 06/2015: BSc Psychology, summa cum laude, University of the Philippines Diliman, PH

Peer reviewed publications


**Manuscripts in preparation**


* Shared first authorship; # Shared senior authorship

**Grants received**

09/2015 – 07/2017: Erasmus Mundus Neurasmus Scholarship: Two-year funding for participation in the Neurasmus Joint Masters Program

03/2018: EMBO Travel Grant: Funding to attend and present a poster at the EMBO Microglia Meeting in Heidelberg, DE

06/2020: FENS-IBRO/PERC Grant: Funding to attend and present a poster at the FENS 2020 Virtual Forum

09/2021: EBBS Travel Grant: Funding to attend and give a talk at the EBBS Meeting in Lausanne, CH

**Oral Presentations**

5/10/2018: Amsterdam Neuroscience Meeting (Amsterdam NL, pecha kucha). *Early-life stress induced vulnerability to develop cognitive dysfunction: a role for astrocytes*

21/06/2019: Dutch Neuroscience Meeting Lunteren (NL). *Early-life stress induced modulation of age-associated changes in mice*

09/06/2021: Dutch Neuroscience Meeting (Online). *Short- and long-term effects of early-life stress on the microglia profile: focus on transcriptome*

04/09/2021: European Brain and Behavior Society Meeting (Lausanne CH). *Early-life stress induced vulnerability to cognitive decline: Glia and their capacity to respond to change*
**Poster Presentations**

16/06/2017: Dutch Neuroscience Meeting (Lunteren NL)

21/03/2018: EMBO Microglia Meeting (Heidelberg DE)

08/06/2018: Dutch Neuroscience Meeting (Lunteren NL)

11/06/2018: International Conference of Molecular Neurodegeneration (Stockholm SE)

04/10/2018: TN2 Meeting (Amsterdam NL)

05/10/2018: Amsterdam Neuroscience Meeting (Amsterdam NL)

17/03/2019: Munich Winter Stress Conference (Munich, DE)

09/05/2019: Venusberg Meeting on Neuroinflammation, third prize (Bonn, DE)

04/10/2019: Amsterdam Neuroscience Meeting (Amsterdam NL)

12/07/2020: FENS 2020 Virtual Forum (online)

21/05/2021: Psychoneuroimmunology Research Society Meeting (online)

30/09/2021: Amsterdam Neuroscience Meeting (online)

13/03/2022: Munich Winter Stress Conference (Munich DE)

16/06/2022: Dutch Neuroscience Meeting (Tiel NL)

**Teaching and organizational experience**

2020 – present: Core team member, Society for Pinoy Neuroscience Enthusiasts (SPiNE), an organization advocating for Philippine neuroscience research [http://fb.com/spine.ph](http://fb.com/spine.ph)

2018 – 2021: Teaching assistant: involved in BS- and MS-level neuroscience courses, supervising student internship projects

03/2018: Brain SIN-posium organization committee [http://brainsinposium.wixsite.com](http://brainsinposium.wixsite.com)

2018-2019: ONWAR committee core team member [http://ONWAR.nl](http://ONWAR.nl)
About the author

Janssen Marcos Kotah was born on the 24th of February, 1995 in Manila, the Philippines. After graduating valedictorian in elementary and high school at the Philippine Cultural College, he pursued a bachelor of science in Psychology at the University of the Philippines Diliman, which he graduated summa cum laude.

Janssen discovered his love for the brain during neuroanatomy sessions as part of a biopsychology class. Although he initially took up psychology as a pre-medical degree, he decided to instead apply for neuroscience masters programs. Fortunately, he was admitted to the Erasmus Mundus Neurasmus Joint Masters Program, which generously funded his study and stay in Europe from 2015 to 2017.

Thanks to Neurasmus, he was able to study at the Charité Medical University in Berlin, as part of the Medical Neurosciences program, as well as the Vrije Universiteit Amsterdam, participating in the research masters for Neurosciences. These programs allowed him to transition into becoming a biologist. In particular, he was drawn to the field of early-life stress, as it presented a path to help out those growing up in adverse conditions, as often happens in countries like the Philippines. In January 2017, Janssen started an internship at the lab of dr. Aniko Korosi and prof. dr. Paul Lucassen at the University of Amsterdam, under the daily supervision of Lianne Hoeijmakers. He obtained both of his MSc degrees in 2017, graduating cum laude from the VU.

In October 2017, Janssen started his PhD at the Korosi lab, continuing the project he worked on as an intern on the effects of early-life stress on aging in mice, as well as initiating and collaborating on several new research lines investigating the effects of early-life stress in both wildtype and transgenic APP/PS1 mice. The findings of these studies, presented in this thesis, have been presented at different national and international meetings, with some also being published in peer-reviewed journals.

Since September 2022, Janssen has been working as a postdoctoral researcher at the University Medical Center Groningen, under the supervision of prof. dr. Bart Eggen and dr. Susanne Kooistra. There, he will be working on cell-cell interactions in multiple sclerosis using different transcriptomic techniques, nurturing the love for glia, R and coding that he developed during his PhD work. Janssen is also very passionate about investing in Philippine neuroscience, and is an active member of the Society for Pinoy Neuroscience Enthusiasts (SPINE), which he co-founded.
Age-dependent impact of early-life stress on glia and synapses

Substrates for increased risk for Alzheimer's disease