BIOGRAPHICAL SKETCH

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NAME: Chandra Ann Reynolds

eRA COMMONS USER NAME (credential, e.g., agency login): creynolds

POSITION TITLE: Professor of Psychology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Irvine	BA	06/1988	Psychology
University of Southern California, Los Angeles	MA, PhD	12/1991, 02/1994*	Developmental Psychology
University of Colorado, Boulder	Postdoctoral	09/1995	Behavioral Genetics
University of Southern California, Los Angeles	Postdoctoral	10/1997	Gerontology
*conferral 05/1994			

A. Personal Statement

With a background in lifespan development and quantitative behavioral genetics, I have applied complex longitudinal and quantitative genetic models to understand variations in cognitive aging, health, and longevity. I have led multi-site collaborative efforts (AG28555), considering the direct and indirect impacts of genes in the cholesterol pathway on intermediate biomarkers and ultimate cognitive and Alzheimer's disease and Alzheimer's disease related (AD/ADRD) phenotypes. I am the contact PI for the NIA-funded grant supporting the evaluation of modifiable risk factors across development and AD/ADRD outcomes for the IGEMS consortium (AG089666, Reynolds, Neiderhiser). I am the contact PI for the *Colorado Adoption/Twin study of Lifespan behavioral development and cognitive aging* (CATSLife, CATSLife2) (AG046938; Reynolds, Wadsworth, MPIs) to evaluate the unique saliency of early life versus proximal factors on adult cognitive maintenance and change. I am an MPI on the VETSA Longitudinal Twin Study of Cognition and Aging (VETSA 4) (AG050595; Kremen, Franz, Panizzon, Elman, Reynolds, MPIs).

Ongoing research that I would like to highlight includes:

Gene-environment interplay among modifiable factors for AD/ADRD: risk and resilience across the lifespan
Reynolds, Neiderhiser (MPIs)
R01AG089666 08/14/2024 - 05/30/2029
Role: PI (Contact)

Colorado Adoption/Twin Study of Lifespan Behavioral Development & Cognitive Aging (CATSLife2)
Reynolds, Wadsworth (MPIs)
2 R01 AG046938   09/15/2020 – 05/31/2025
Role: PI (Contact)

The VETSA Longitudinal Twin Study of Cognition and Aging (VETSA 4)
Kremen, Franz, Pannizon, Elman, Reynolds (MPI's)
5 R01 AG050595   06/01/2020 - 03/31/2025

Role: Co-Investigator (2020-2023) and MPI (2023-present)

Relevant research that I would like to highlight includes:

Karlsson, I. K., Escott-Price, V., Gatz, M., Hardy, J., Pedersen, N. L., Shoai, M., & **Reynolds, C. A.** (2022). Measuring heritable contributions to Alzheimer's disease: polygenic risk score analysis with twins. *Brain Commun, 4*(1), fcab308. doi:10.1093/braincomms/fcab308

Mak, J. K. L., Kuja-Halkola, R., Bai, G., Hassing, L. B., Pedersen, N. L., Hagg, S., Jylhava, J., & **Reynolds, C. A.** (2023). Genetic and Environmental Influences on Longitudinal Frailty Trajectories From Adulthood into Old Age. *J Gerontol A Biol Sci Med Sci, 78*(2), 333-341. doi:10.1093/gerona/glac197 [PMC9951061]

Zheng, A., Friedman, N. P., Gustavson, D. E., Corley, R. P., Wadsworth, S. J., & **Reynolds, C. A.** (2024). Lifestyle and psychosocial associations with cognition at the cusp of midlife using twins and siblings. Alzheimers Dement (Amst), 16(3), e12609. doi:10.1002/dad2.12609

B. Positions, Scientific Appointments, and Honors
Positions

August 2023 -	Professor of Psychology and Neuroscience and Fellow of the Institute for Behavioral Genetics (IBG), University of Colorado Boulder
June-August 2023	Visiting Professor, University of Colorado Boulder [Note. June 2023 unpaid]
July 2023 -	Professor Emerita of Psychology, University of California, Riverside
2021-	Affiliated faculty, Graduate Program in Genetics, Genomics & Bioinformatics, University of California, Riverside
2017-2022	Affiliated faculty, Center for Geospatial Sciences (CGS),University of California, Riverside
2011-2023	Professor of Psychology, University of California, Riverside
2006-2011	Associate Professor of Psychology, University of California, Riverside
2001-2006	Assistant Professor of Psychology, University of California, Riverside
1997-2000	Research Assistant Professor/Research Associate, University of Southern California
1995-1996	Research Associate, Department of Psychology, University of Southern California
1992	Visiting Researcher, Karolinska Institute, Stockholm

Scientific Appointments

Fellow

2022 - present	Fellow, Center for Economic and Social Research (CESR), University of Southern California (07/2022)

Editorial

2008-present	Associate Editor, *Behavior Genetics*
2016/17-20	Consulting Editor, *Developmental Psychology*
2017-22	Review Editor, *Frontiers in Genetics, Behavioral and Psychiatric Genetics*

Committees/ Panels

2007- present	NIH Peer Review. BGES: 10/09 to 06/13 (*ad hoc*: 10/07, 02/08); SEP: *ad hoc* 01/09, 10/17, 03/18, 02/19; SSPB: *ad hoc* 02/16. NIA P01: *ad hoc* 10/11, 06/12, 10/24; NIA U01 *ad hoc* 05/19, 06/20, 10/23; NIA U19 *ad hoc* 06/22 (chair); NIA U24 *ad hoc* 01/17, 05/19.
2022-23	NIA Early (Neuro)Psychological Changes in AD/ADRD Project webinar series: (A) Invited presenter [November 2022, "Assessment of Neuropsychological Change Across the Lifespan"[and (B) participant [December 2022 - April 2023, various topics].
2019	Invited Panelist: University of California – Nanyang Technological University Singapore Joint Workshop on Healthy Aging

2017	Invited participant: A Workshop Co-sponsored by NIEHS and NIA: "Telomeres as Sentinels for Environmental Exposures, Psychosocial Stress, and Disease Susceptibility"
2013	Invited sub-committee participant: National Advisory Council on Aging (NACA) review of the NIA's BSR section: "Behavioral and Social Aspects of the Genetics of Aging"
2012	Invited presenter and panel participant: Institute of Gerontology, Jönköping University, Sweden, Workshop on "Ageing – Living Conditions and Health"
2010	Invited presenter and panel participant, NAS & NIA's: "Using GWAS to Explore Fundamental Questions about Aging in the Health and Retirement Study (HRS) Sample".
2007	Invited participant: NIA's 'Planning Meeting for the Genetics of Alzheimer's Disease'.

Honors

2020	Fellow, Academy of Behavioral Medicine Research
2019	Fellow, Association for Psychological Science
2013	Fellow, Gerontological Society of America
2012	PhD *honoris causa*, Jönköping University, Sweden
2003	Faculty of the Year, UC Riverside Psychology Department
1997	Los Angeles Alzheimer's Association, Turken Scholarship Award recipient

C. Contributions to Science

1. My early publications challenged and refined understandings of the **measurement and etiology of cognitive decline**. At the time of my entry into cognitive aging research, the quantitative approaches applied to measuring cognitive change varied considerably and relatively little was known about the genetic and environmental etiologies of normative cognitive change. Initial work included a comparison of quantitative methods to address cognitive change, suggesting superiority of random effect approaches to other extant approaches at the time including annualized difference scores estimates, criterion-based methods, and two-stage least squares approaches. Applying random effects growth models to cognitive change across six years suggested, surprisingly, the primary importance of stochastic influences for entry into decline. Yet, unconvinced and challenged by dementia and AD findings, expanded examinations with longer follow-up suggested a nuanced set of findings: nonlinear change is moderately heritable in comparison to linear change and etiological contributions vary across age and domain.

   a) Reynolds, C. A., Gatz, M., & Pedersen, N. L. (2002). Individual variation for cognitive decline: Quantitative methods for describing patterns of change. *Psychology & Aging, 17*(2), 271-287.
   b) Reynolds, C.A., Finkel, D., McArdle, J.J, Gatz, M., Berg, S. & Pedersen, N.L. (2005). Quantitative genetic analysis of latent growth curve models of cognitive abilities in adulthood. *Developmental Psychology, 41*, 3-16.
   c) Reynolds, C.A., Fiske, A., Fratiglioni, L., Pedersen, N.L., & Gatz, M. (2006). Heritability of an age-dependent categorical phenotype: Cognitive dysfunction. *Twin Research & Human Genetics, 9*, 17-23.
   d) Ricker, A. A., Corley, R., DeFries, J. C., Wadsworth, S. J., & Reynolds, C. A. (2018). Examining the Influence of Perceived Stress on Developmental Change in Memory and Perceptual Speed for Adopted and Nonadopted Individuals. *Dev Psychol, 54*(1), 138-150. [PMC5750082]

2. Working with a team of collaborators, I have led and participated in efforts to **consider molecular genetic markers that underlie the genetic and environmental etiologies of cognitive change trajectories**. Early on, it was far less applied to quantitative traits measured in normative samples over multiple waves, and even less so using a twin approach. The *SORL1* study was the first to demonstrate association of risk set scores on longitudinal cognitive trajectories across domains; the results suggested a divergence of effects on cognitive change, not only dependent on the location of risk variants but with respect to effects for men and women. Recent work includes larger collaborative efforts including work on multiple variants and genetic risk scores.

   a) Reynolds, C.A., Jansson, M., Gatz, M., & Pedersen, N.L. (2006). Longitudinal change in memory performance associated with HTR2A polymorphism. *Neurobiology of Aging, 27*, 150-4.
   b) Reynolds, C.A., Prince, J.A., Feuk, L., Gatz, M., & Pedersen, N.L. (2006). Longitudinal memory performance during normal aging: twin association models of *APOE* and other Alzheimer candidate genes. *Behavior Genetics, 36*, 185-94.

c) Davies, G., Harris, S. E., Reynolds, C. A., Payton, A., Knight, H. M., Liewald, D. C., Lopez, L. M., Luciano, M., Gow, A. J., Corley, J., Henderson, R., Murray, C., Pattie, A., Fox, H. C., Redmond, P., Lutz, M. W., Chiba-Falek, O., Linnertz, C., Saith, S., Haggarty, P., McNeill, G., Ke, X., Ollier, W., Horan, M., Roses, A. D., Ponting, C. P., Porteous, D. J., Tenesa, A., Pickles, A., Starr, J. M., Whalley, L. J., Pedersen, N. L., Pendleton, N., Visscher, P. M., & Deary, I. J. (2014). A Genome-Wide Association Study Implicates the Apoe Locus in Nonpathological Cognitive Ageing. *Mol Psychiatry, 19*(1), 76-87. [PMC7321835]
d) Reynolds, C. A., Zavala, C., Gatz, M., Vie, L., Johansson, B., Malmberg, B., Ingelsson, E., Prince, J. A., & Pedersen, N. L. (2013). Sortilin receptor 1 predicts longitudinal cognitive change. *Neurobiology of Aging, 34(6),1710.e11-8. doi: 10.1016/j.neurobiolaging.2012.12.006.* [PMC3839667]

3. With a team of collaborators, I have sought to further demonstrate the genetic and environmental etiologies of cognitive dysfunction and dementia by **considering direct and indirect impacts of genes in the cholesterol pathway on intermediate lipid biomarkers and contributions to cognitive decline and dementia** (e.g., lipid and immune/inflammatory pathways). Various strategies were applied, including discordant twin pair analysis, logistic regression and survival models, and pathway and whole gene methods to consider gene associations with lipids, cognitive change, and dementia. Overall, findings from the cholesterol pathway work suggest that while serum lipid levels are predictive of cognitive decline and dementia, an increasingly complex picture was evident vis-à-vis: the relative lack of enrichment of cholesterol pathway variants on AD and dementia risk with some notable exceptions, the unique effects of *APOE* variants on LDL lipid levels versus dementia risk, and sex and age moderation of lipid-cognitive trajectory relationships. More recently, collaborators and I observed a possible role of *APOE* on IQ in childhood and adolescence. Last, recent work incorporating polygenic scores into twin models suggest *APOE* dominates the measurable polygenic risk but that much remains to be learned about the remaining unmeasured heritable variation contributing to Alzheimer's disease.
   a) Reynolds CA, Gatz M, Prince JA, Berg S, Pedersen NL. (2010). Serum lipid levels and cognitive change in late life. *Journal of the American Geriatrics Society, 58*, 501-509. [PMC2913576]
   b) Reynolds, C. A., Gatz, M., Pedersen, N. L., & Prince, J. A. (2011). An assessment of CETP sequence variation in relation to cognitive decline and dementia risk. *Int J Mol Epidemiol Genet, 2*(2), 122-129. [PMC3110386]
   c) Reynolds, C. A., Smolen, A., Corley, R. P., Munoz, E., Friedman, N. P., Rhee, S. H., Stallings, M. C., DeFries, J. C., & Wadsworth, S. J. (2019, Dec). *APOE* effects on cognition from childhood to adolescence. *Neurobiol Aging, 84*, 239.e231-239.e238. [PMC6800620].
   d) Karlsson, I. K., Escott-Price, V., Gatz, M., Hardy, J., Pedersen, N. L., Shoai, M., & Reynolds, C. A. (2022). Measuring heritable contributions to Alzheimer's disease: polygenic risk score analysis with twins. *Brain Communications, 4*(1), fcab308. doi:10.1093/braincomms/fcab308. [PMC8833403]

4. Evaluating **sensitive periods where genetic-environmental synergies may be most salient to health behaviors and cognitive functioning** are important not only in early development but whether and when resurgent periods in late adulthood occur. With colleagues and students, I have led and participated in efforts to capitalize on the strengths of multi-decade longitudinal data to elucidate phenotypic and etiological relationships between potentially modifiable health and socio-emotional factors, cognitive aging, and longevity. For example, work on intra-pair MZ differences in cognitive trajectories was the first to demonstrate GxE interaction processes for cognitive trajectories: (1) gene variants implicated in the regulation of serotonin, estrogen, and cholesterol (e.g., *APOE*), were associated with increased within-pair divergence in memory trajectories; and (2) divergence in trajectories were further amplified by synergies with environmental sequelae of depression for those at low genetic risk (e.g., non-*APOE* e4). Other work has demonstrated the multi-factorial nature of early life and proximal influences on health, including unique pathways for men and women.
   a) Reynolds, C. A., Gatz, M., Christensen, K., Christiansen, L., Dahl Aslan, A. K., Kaprio, J., Korhonen, T., Kremen, W. S., Krueger, R., McGue, M., Neiderhiser, J. M., Pedersen, N. L., for the IGEMS consortium (2016). Gene-Environment Interplay in Physical, Psychological, and Cognitive Domains in Mid to Late Adulthood: Is *APOE* a Variability Gene? *Behav Genet, 46*(1), 4-19. 10.1007/s10519-015-9761-3 [PMC4858319]
   b) Zavala, C., Beam, C. R., Finch, B. K., Gatz, M., Johnson, W., Kremen, W. S., Neiderhiser, J. M., Pedersen, N. L., & Reynolds, C. A. (2018). Attained SES as a Moderator of Adult Cognitive Performance: Testing Gene-Environment Interaction in Various Cognitive Domains. *Dev Psychol, 54*(12), 2356-2370.http://dx.doi.org/10.1037/dev0000576. [PMC6263814]

c) Karlsson, I. K., Gatz, M., Arpawong, T. E., Dahl Aslan, A. K., & Reynolds, C. A. (2021). The dynamic association between body mass index and cognition from midlife through late-life, and the effect of sex and genetic influences. *Sci Rep, 11*(1), 7206. doi:10.1038/s41598-021-86667-4. [PMC8010114].
d) Luna, M. G., Pahlen, S., Corley, R. P., Wadsworth, S. J., & Reynolds, C. A. (2023). Frailty and Processing Speed Performance at the Cusp of Midlife in CATSLife. J Gerontol B Psychol Sci Soc Sci, 78(11), 1834-1842. https://doi.org/10.1093/geronb/gbad102. [PMC10645312].

5. With a team of collaborators, I have sought to further evaluate **longitudinal dynamics of biomarkers that may track biological aging and index gene-environment interplay.** I have led and participated in efforts to understand the etiologies of longitudinal DNA methylation, a measure of epigenetic processes that produce altered gene expression due to environmental exposures. I have also participated in studies evaluating the etiologies of longitudinal telomere lengths and associations of telomere lengths with cognition and health endpoints. The methylation work represents the first longitudinal biometrical studies to show heritable influences on variation in methylation age across time measured with two epigenetic 'clocks'. Moreover, results of individual methylation sites (CpGs) across the methylome suggest aging-related sites may be more heritable than background sites in aging twins. Genetic influences contribute to stability in methylation age across a decade but person-specific environments increase in importance suggesting that change in rates of biological aging may be sensitive to environmental experiences.
a) Zhan, Y., Clements, M. S., Roberts, R. O., Vassilaki, M., Druliner, B. R., Boardman, L. A., Petersen, R. C., Reynolds, C. A., Pedersen, N. L., & Hagg, S. (2018). Association of Telomere Length with General Cognitive Trajectories: A Meta-Analysis of Four Prospective Cohort Studies. *Neurobiol Aging, 69*, 111-116. 10.1016/j.neurobiolaging.2018.05.004. [PMC6064381]
b) Jylhava, J., Hjelmborg, J., Soerensen, M., Munoz, E., Tan, Q., Kuja-Halkola, R., Mengel-From, J., Christensen, K., Christiansen, L., Hagg, S., Pedersen, N. L., & Reynolds, C. A. (2019). Longitudinal Changes in the Genetic and Environmental Influences on the Epigenetic Clocks across Old Age: Evidence from Two Twin Cohorts. *EBioMedicine, 40*, 710-716. [PMC6413471]
c) Reynolds, C. A., Tan, Q., Munoz, E., Jylhava, J., Hjelmborg, J., Christiansen, L., Hagg, S., & Pedersen, N. L. (2020, Jul 24). A decade of epigenetic change in aging twins: Genetic and environmental contributions to longitudinal DNA methylation. *Aging Cell*, e13197. https://doi.org/10.1111/acel.13197 [PMC7431820].
d) Mak, J. K. L., Karlsson, I. K., Tang, B., Wang, Y., Pedersen, N. L., Hagg, S., Jylhava, J., & Reynolds, C. A. (2023). Temporal dynamics of epigenetic aging and frailty from midlife to old age. *J Gerontol A Biol Sci Med Sci*. doi:10.1093/gerona/glad251 [PMC11421301]

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