## 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)* | Start Date MM/YYYY | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|---|
| University of California, Irvine | BA | 1983 | 1988 | Psychology |
| University of Southern California, Los Angeles | MA, PhD | 1989 | 1991, 1994 | Developmental Psych. |
| University of Colorado, Boulder | Postdoctoral | 1994 | 1995 | Behavioral Genetics |
| University of Southern California, Los Angeles | Postdoctoral | 1996 | 1997 | Gerontology |

### 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 direct and indirect impacts of genes in the cholesterol pathway on intermediate biomarkers and ultimate cognitive phenotypes measured in four related twin samples. I have led or participated in projects on childhood and social factors that predict life course patterns of health, well-being, cognition and longevity (AG02700; Terman Life Cycle Study; HD010333, Colorado Adoption Project [Wadsworth, PI]). I am a co-investigator and site PI for NIA funded projects for the IGEMS consortium [AG060470 (Gatz/Pedersen); AG059329 (Pedersen/Finch/Gatz)]. I am a co-I on the VETSA Longitudinal Twin Study of Cognition and Aging (VETSA 3, VETSA 4) (AG018386; Kremen, Lyons, Franz, MPIs). I serve as contact PI of the MPI project *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.

Ongoing research that I would like to highlight include:

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, Lyons, Franz (MPI's)
2 R01 AG018386 06/01/2020 - 03/31/2025
Role: Co-Investigator and Site PI

Clarify risk and protective factors for dementia with the Interplay of Genes and Environment in Multiple Studies (IGEMS) consortium
Gatz/Pedersen
R01 AG060470 09/01/18 – 03/31/23
Role: Co-Investigator and Site PI

SES Health Gradients in Late Life: Testing Models of Gene-Environment Interplay in an International Twin Consortium
Pedersen/Finch/Gatz
R01 AG059329 09/01/18 – 05/31/23
Role: Co-Investigator and Site PI

Relevant research that I would like to highlight includes:

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].

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].

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].

**B. Positions, Scientific Appointments and Honors**

**Positions**

| | |
|---|---|
| 2021-present | Affiliated faculty, Graduate Program in Genetics, Genomics & Bioinformatics, University of California, Riverside |
| 2017-present | Affiliated faculty, Center for Geospatial Sciences (CGS),University of California, Riverside |
| 2011-present | 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 - | Fellow, Center for Economic and Social Research (CESR), University of Southern California (07/2022) |
| *Editorial* | |
| 2016/17-20 | Consulting Editor, *Developmental Psychology* |
| 2017- | Review Editor, *Frontiers in Genetics, Behavioral and Psychiatric Genetics* |
| 2008- | Associate Editor, *Behavior Genetics* |
| *Committee Service* | |
| 2007-2022 | NIH Peer Review Committees. 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.<br>NIA P01: ad hoc 10/11, 06/12; NIA U01 ad hoc 05/19, 06/20; NIA U19 ad hoc 06/22 (chair); NIA U24 ad hoc 01/17, 05/19. |
| 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. Recent work includes larger collaborative efforts including work on multiple variants and genetic risk scores. 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.

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.
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

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., Berg, S., Pedersen, N.L. (2007). Genotype-Environment Interactions: Cognitive Aging and Social Factors. *Twin Research and Human Genetics*, *10*, 241-254.
b) 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].
c) 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]
d) 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

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) Berglund, K., Reynolds, C. A., Ploner, A., Gerritsen, L., Hovatta, I., Pedersen, N. L., & Hagg, S. (2016). Longitudinal Decline of Leukocyte Telomere Length in Old Age and the Association with Sex and Genetic Risk. *Aging (Albany NY), 8*(7), 1398-1415. 10.18632/aging.100995. [PMC4993338]
b) 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]
c) 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]
d) 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].

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