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COGA NEWSLETTER

In This issue:

Introduction to the second issue from Laura Bierut, M.D., Principal Investigator at Washington University (WashU) in St. Louis:

"The COGA study has adapted as technologies have changed, and our scientific knowledge has grown. In the beginning of COGA, we sent letters to people's homes and called potential participants on their landlines. Now we use emails and text messages to communicate, which are often faster and more efficient. In addition, many of the questionnaires are now computerized, which allows faster and more accurate data collection.

The greatest change has been in the genetic discoveries that COGA has been involved in. When COGA started, we only knew that variation in alcohol metabolizing genes altered an individual's risk of developing alcohol related problems. Genetic technologies now enable us to study a person's entire genetic code for only a few hundred dollars. This technology advancement has ushered in the ability to study millions of people. Now we know of hundreds of different genetic regions that influence how much people drink and whether they develop alcohol use disorder (AUD).

The next challenge is how we harness this information about hundreds of genetic regions changing a person's risk of developing AUD. How do we gain more knowledge about what is really happening in the brain so that we can better prevent and treat this disorder? "

HARNESSING GROWTH THROUGH TECHNOLOGY INNOVATION

Laura Bierut, MD.

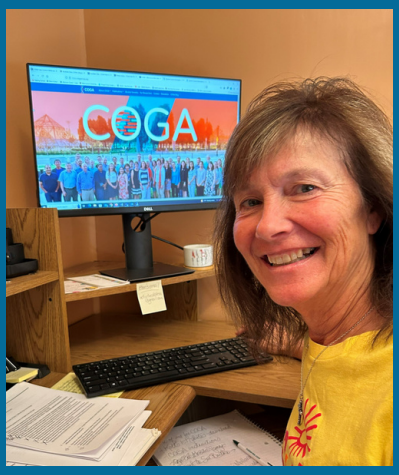
Meet the Washington University Team!

Haleigh Niles. B.S. (Interviewer) and Roz Abdulqader, B.S. (Site Manager, oversees recruitment and data collection)

Scott Saccone, Ph.D, Webmaster for the COGA website

Lingwei Sun, Senior Analyst, is responsible for central data collection, storage, and distribution at the WashU data core.

Sue Winkeler, B.A., Senior Data Control Coordinator, maintains and updates the COGA websites. She is currently combining two separate websites (for the current Lifespan Project and for earlier phases) together in one place.



RECRUITMENT ACROSS THE DECADES

Sherri Fisher, M.S., longtime Research Administrator for COGA

How has recruitment evolved over the years?

"When the study began, participants were recruited from inpatient alcohol treatment facilities. Detailed family pedigrees were created, and then relatives were invited to participate. Comparison families were also recruited from the community through methods/locations that varied by site. That phase of the study lasted for about 10 years. A 5-year follow up study was then undertaken, and families were extended further with additional relatives invited; this phase also lasted for approximately 10 years. By this time we had recruited thousands of participants at 6 sites across the country. For the next 10 years, we focused on multiple follow-up assessments with adolescents and young adults already in our sample of COGA families to study changes over this important developmental period. For the past 4 years, we have been recruiting adults in mid-life and late-life who have previously participated in the study. So it has been many years since COGA recruited “new” participants. We are so thankful to our families who remain committed to COGA and enable this important research to continue."

[More information on Data Collection and the Lifespan project]

John Rice, Ph.D, principal statistican and data manager with COGA at WashU since 1989.

How has the COGA study changed during your time?

"From a genetics perspective, the initial methodology was genetic linkage, using a few hundred markers to examine the co-occurrence of AUD with the genetic markers. This required us to sample large, densely affected pedigrees as well as control families. In 2005, there was a shift from examining linkage to studying association, using chips that typed hundreds of thousands of genetic markers to help identify susceptibility genes. All the COGA subjects with DNA have been genotyped using this newer method."

STAYING CURRENT WITH THE TIMES

How has COGA adapted to technology and incorporated that in the study?

"COGA has adopted new state-of- the-art genetic approaches. COGA is unique in that it has well characterized families ascertained through cases identified in treatment centers and followed over time. Today, there are several large representative samples (e.g., the UKBiobank in the UK) with Genome-Wide-Association data (GWAS). These additional samples are useful in the analysis of our clinical sample, and we have made use of these new studies and new genetic methods (such as polygenic risk scores) that derive risk measures from these representative samples and then apply and test them on COGA data."

Participant Comments

COGA participants from WashU share their thoughts on their inolvement and the study's impact.

"LOOKING FORWARD TO FOLLOWING (THIS STUDY'S PROGRESS). IT WAS VERY COOL PARTICIPATING IN THE STUDY."

"IT MAKES ME FEEL THAT I AM HELPING IN SOME WAY."

"MY PARTICIPATION COULD HELP IN FINDING OUT WHY SOME (PEOPLE) TURN TO ALCOHOL, WHETHER THAT IS HEREDITARY, AND SEEING HOW IT CAN BE AVOIDED."

YOUNG INVESTIGATORS HELP DRIVE WASHINGTON UNIVERSITY'S CUTTING-EDGE RESEARCH

Alex Miller, a postdoctoral fellow at WashU, has investigated specific symptoms that most strongly predict the likelihood of developing severe Alcohol Use Disorder (AUD). He has found that, among young adults with mild or moderate AUD, those who experienced alcohol withdrawal and other particular symptoms were at greater risk of progressing to severe AUD.

Sarah Paul, a psychology Ph.D student at WashU, has examined the connections between internalizing (e.g., depression) and externalizing symptoms (e.g., ADHD) and specific stages of problematic alcohol involvement. She found that externalizing symptoms are linked with all stages, from mild to severe. In contrast, internalizing symptoms are mostly connected to later-stage, more severe AUD.

Emma Johnson, Ph.D, is an Assistant Professor in Psychiatry at WashU and has been working with the COGA project since she began her postdoc in 2017. She is interested in understanding why alcohol use disorder and other substance use disorders often occur with each other and with other psychiatric disorders (such as schizophrenia). Emma recently published a study that found that greater genetic risk for schizophrenia is also associated with an increased likelihood of psychotic-like experiences from using marijuana, such as feeling paranoid, experiencing cognitive difficulties, or distancing oneself from family and friends. This study was only possible because of the rich behavioral and genetic data available in the COGA project.

Mer Francis, Ph.D, MSW, recently moved from WashU and is now an Assistant Professor at Virginia Commonwealth University. They are interested in how people's social networks and family history of substance use affect recovery. Dr. Francis has found that people with stronger and more extensive supportive relationships are less likely to develop an alcohol use problem, and, if they do, are more likely to recover. Read more about Mer's work here: https://socialwork.vcu.edu/directory/mer-francis-profile/

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WASH U'S ESTABLISHED RESEARCHERS EXAMINE A BROAD RANGE OF INFLUENCES ON THE ONSET AND COURSE OF ALCOHOL PROBLEMS

Kathleen Bucholz, PhD, is currently Co-Director of the Lifespan Project and has helped steer COGA's course since the study's inception in 1989. She has played a key role in the design, selection, and testing of the study's core interview and questionnaires at each phase of the project. Illustrative of her work are studies focused on identifying specific subtypes of alcohol problems, as well as those increasing our understanding of the progression of alcohol and other drug problems from first use, to problem use, to outright disorder. She is grateful to all COGA participants, for their willingness to answer the many questions in the interviews and complete the laboratory studies over multiple occasions; these provide the information for increased understanding of the spectrum of substance involvement and related behaviors. She also appreciates collaborating with expert and generous colleagues across all sites to further the scientific accomplishments of COGA.

Arpana Agrawal, PhD, joined the COGA site in St. Louis as a postdoctoral researcher. She is currently the Scientific Director and co-leads the Genomics Project. Her research focuses on understanding how genetic factors contribute to various aspects of alcohol use, and the relationship between heavy or problematic alcohol use and other mental and physical health behaviors. The unique multigenerational families that participate in COGA have allowed her to learn so much about how nature and nurture shape our behaviors. She feels most fortunate for her colleagues, both at Washington University and at other COGA sites, for their intellectual generosity and for every COGA participant that has taken the time to contribute to this important scientific endeavor.

Vivia McCutcheon, Ph.D, has worked as a COGA Co-Investigator since 2008. She has found that parental AUDs increase risk that their children will start to use alcohol early and develop their own AUDs. Dr. McCutcheon has also discovered that individuals with AUD are more likely to remit - meaning they stop experiencing symptoms of AUD - if they have a 1st-degree relative who has also remitted. She is currently examining other influences on remission and relapse in AUD, including major life events (e.g., marriage), drug and psychiatric problems, genes, trauma, and treatment. Vivia is grateful for the wealth of information participants have contributed to COGA and the expertise of other COGA researchers that make these investigations possible.

Andrey Anokhin, Ph.D, oversees neurophysiological (EEG) assessments of COGA participants at the Washington University site. He analyzes brain electrical activity (brain waves) recorded during different cognitive tasks to measure neural signatures of attention, decision making, and detection of errors – the brain's "oops!" response – to better understand how brain functions change across the lifespan and what role alcohol plays in brain and cognitive aging.

Sarah Hartz, M.D., PhD, is a psychiatrist and statistician with experience in genetics and the distribution and causes of substance use disorder. Her current work focuses on the interplay between alcohol use and Alzheimer disease and the communication of research results to participants. In COGA, she is working on standardized cognitive measures to use in the assessment of older individuals and measuring biomarkers (e.g., genes, EEG patterns) that predict Alzheimer disease onset and progression. In addition, she is working with John Rice to become the next director of the data management core.

Progress

COGA continues to build its database, thanks to the contribution of many participants. The more data we gather from our participants, the more accurate and helpful our findings are. Since COGA began in 1989, we have collected information from more than 17,000 individuals. Below is a figure that shows the number of interviews we have conducted for the current COGA Lifespan Project, which began in 2019. [More information on Data Collection and the Lifespan project]

THE TOTAL NUMBER OF PARTICIPANTS EVALUATED HAS INCREASED BY 30% IN THE PAST YEAR!

Research Highlights (click on titles for more details)

Genetic Nurture Effects for Alcohol Use Disorder

This investigation focused on two different ways parents' negative relationship to each other can increase risk for later alcohol use by their adolescent offspring. Divorce and general discord in the parents' relationship can lead to a chaotic household and serve as an environmental risk factor for the development of problems in the child. In addition, a second path may be biological -- some of the parents' genes that contributed to their own fighting may be inherited by the child and raise their risk of alcohol problems. In this study, there was evidence for both pathways contributing to the offspring's risk of drinking regularly -- and becoming drunk -- at an earlier age, as well as developing more drinking problems as an adult.

Influence of Parental Alcohol Dependence Symptoms and Parenting on Adolescent Risky Drinking and Conduct Problems: A Family Systems Perspective

This study examined ways in which parents' alcohol dependence can influence their adolescent child's drinking and behavioral problems. It focused on whether mothers' and fathers' alcohol dependence might have different effects on their child's outcome, and if these effects are partly due to alcohol limiting their ability to be an effective parent. The authors looked at parental involvement with their child, parent-child communication as well as parent-child closeness. Results suggest that fathers' alcohol dependence worsens the outcome of adolescents' drinking and conduct problems by undermining both the fathers' and the mothers' ability to be an effective parent. Mothers' alcohol dependence, on the other hand, was not found to influence adolescent drinking or conduct problems by compromising parenting behaviors. Ethnic background did not play a role in any of these findings.

Positive Parenting, Brain Development, and Teen Alcohol Use

This investigation looked at the effect of "positive parenting" on teenagers' binge drinking and brain development, two factors that can lead to later alcohol problems. Evidence of positive parenting was measured by how close the parent and the adolescent reported their relationship in separate interviews. Assessment of brain development was based on EEG measures. It was found that a close relationship with an adolescent may indeed protect them against binge drinking, which could in turn reduce the chance of other alcohol problems down the road. The parents' and adolescents' gender also played a role: closeness to the father predicted healthier brain function, particularly among sons, while closeness to the mother predicted less binge drinking among daughters.

OUR THANKS TO COGA PARTICIPANTS, WHO HAVE CONTRIBUTED THEIR VALUABLE TIME AND INFORMATION SINCE 1990!

Newsletter created at the Iowa COGA Site by John Kramer, Morgan Tyma, Bethany Marenna, Tina Cronbaugh, with information provided by the COGA staff at WashU.