**COGA NEWSLETTER** 

March 2023

Collaborative Study on the Genetics of Alcoholism

# WELCOME!

We are delighted to share with you our new newsletter for the Collaborative Study on the Genetics of Alcoholism (COGA) study, a project that has targeted the genetics of alcoholism for over 30 years. We plan to update this newsletter periodically to share with our research participants (and others) additional information about sites, productivity, and research.

We are grateful to our families who have participated in the COGA study over the years some include individuals with alcohol problems, while other families do not. Through their dedication we have been able to better understand how alcohol use disorders affect individuals and families across the lifetime. We also have been able to better define risk factors that increase the chance of future alcohol use disorders and to identify factors that decrease this risk. As a wider range of substance use has become more common, we have also extended the scope of COGA to address the genetics of a variety of drugs to better understand how the use of one substance affects the use of others. With the ongoing COVID pandemic, we have tried to better understand its effect on the use of alcohol and other substances and its impact on our research participants.

We look forward to receiving feedback from you regarding the newsletter topics that you find most interesting as well as areas that you hope the newsletter could address in future issues.



#### https://cogastudy.org/

## Site Spotlight - Iowa

Learn more about the lowa site, what they do, and who they are!

### What kinds of studies and findings has lowa been involved in?

Over the years, lowa has looked at a number of topics. Dr. Kuperman and Dr. Kramer have backgrounds in child and adolescent problems, so we have explored how they combine with certain genes to predict alcohol misuse. As one example, we have focused on predictors of when young people start to drink. Some of the strongest predictors of early drinking we found were how many of their friends drink and how many family members had alcohol use disorders. Other areas of interest have included the complex connections between anxiety, depression, and alcohol problems.



From left to right: Bethany Marenna, John Kramer, Angie Cookman, Sam Kuperman, former Iowa site members Shizhong Han and Xiangtao Liu.

#### What do you hope to achieve in the future? What projects are you working on?

Taking the same approach used to predict alcohol initiation, we are starting to identify predictors of illegal opioid use. Another current project is the relationship between alcohol problems and when and why participants die. In addition, we are examining blood samples collected from Iowa participants in the 1990's to see whether these samples are related to health and cognitive problems they have today, more than 25 years later.

At lowa, we have had a longstanding interest in internalizing problems such as anxiety and depression (<u>more information about Internalizing characteristics</u>). We are identifying genes that contribute to these internalizing characteristics. We are also looking at the combined effect of internalizing and externalizing disorders on alcohol and drug use, focusing on individuals who have high levels of both characteristics.

In addition, we are targeting factors that are related to increased use of drugs and alcohol during COVID. One possible characteristic is "negative urgency", the tendency to turn to drugs and alcohol when experiencing negative emotions like anger and anxiety. We are looking to see whether stress from COVID has this effect on substance use in individuals who have high levels of negative urgency.

Finally, the Iowa team has found developing this newsletter to be an exciting challenge. We look forward to publishing more issues this year and making improvements based on feedback from you, the readers.

#### **Meet the Iowa Team!**

We asked the lowa team what they most liked about their role. Here are their responses:

Sam Kuperman M.D., Iowa's Principal Investigator from the very beginning of COGA in 1989: "Because we are a small group at Iowa and have been here many years, we know each other well and can solve most problems and day to day issues quickly. I am proud to be part of a group that is dedicated to the study of alcohol and substance problems. COGA investigators are experts from many fields (e.g., therapists, psychologists, geneticists, statisticians), and the combination of their expertise leads to cutting edge research."



From left to right at a national COGA meeting: Sam Kuperman, Grace Chan, Leah Wetherhill (Indiana), John Kramer

**John Kramer, Ph.D.**, Co-Principal Investigator and Project Manager, has been at Iowa since 1990: "Number one is my co-workers at Iowa. I also enjoy joining forces with other COGA members who contribute to this project: expert interviewers and EEG administrators, highly skilled data managers, and talented researchers who look at everything from the effect of divorce on alcohol problems to how brain cells are affected by exposure to alcohol. My job hits the sweet spot—it is stimulating but not too stressful."

Angie Cookman, B.A., Iowa's Principal Interviewer, joined COGA when participants were first seen in 1990: "I personally find great satisfaction in working with this wonderful group of researchers. This has led to close friendships that continue to this day. I have enjoyed getting to know our 230 families over the years; the multi-generational aspect of this job makes it particularly satisfying. I like collaborating with my co-workers, collecting data for our researchers."



From left to right: Sam Kuperman, Angie Cookman, Bethany Marenna

**Grace Chan, Ph.D.**, our Statistician and Data Manager, began here in 2004, then relocated to the New England Area, where she joined the Connecticut COGA site, but continues to work with us remotely: "I enjoy and value the opportunity to learn about the addiction field and apply statistics to address research questions using the rich COGA databases."

**Bethany Marenna, M.A.**, EEG (brain wave) Administrator, has been a part of our site since 2000: "I really enjoy working with our research participants. The EEG is not necessarily an easy task. I enjoy the conversations I have with them to help them put them at ease."

## **Progress Figures**

COGA continues to build its database, thanks to the contribution of many participants. The more data we gather, the more accurate and helpful our findings are. Since COGA began in 1989, we have collected information from almost 18,000 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 about Data Collection and the Lifespan Project).



#### **Iowa Participant Comments**

"I believe I have been in this study since 1992; total of 31 years. The hope that I have, in this project, is that it helps alcoholics and/or professionals in dealing with this disease. I have hope that at least one person may be helped, and that's worth it!" " My family and I have been in the COGA study for many years... As a recovering alcoholic myself, it feels important to be a part of this information gathering... [It] will be helpful to families, researchers, teachers, etc. That is why I'm here."

#### WHAT IS "INTERNALIZING AND EXTERNALIZING BEHAVIOR?"

#### AND WHAT DO GENES HAVE TO DO WITH IT?

Click the article titles to learn more!

### **Research Highlights**

One aspect of human behavior that COGA researchers have looked at in relation to alcohol use is how an individual processes negative emotions like anger. Do they express these emotions by acting out impulsively or aggressively—or do they keep these emotions inside? These tendencies are partly inherited and partly learned. The major internalizing disorders include depression and anxiety disorders. Externalizing behaviors and disorders include disruptive and aggressive behavior, ADHD, risky sexual behavior, impulse spending, and substance use disorders. The articles below are three examples of findings published by COGA scientists. For more articles and information on Internalizing and Externalizing behaviors and disorders, please see:

> Exploring Externalizing Behavior in COGA Exploring Internalizing Behavior in COGA



<u>The Role of Parental Genotype in the</u> <u>Intergenerational Transmission of</u> <u>Externalizing Behavior: Evidence for</u> <u>Genetic Nurturance</u>

Findings from this study suggest that a parent's genes influence their offspring's externalizing behavior directly by contributing to the offspring's genetic makeup. But, they also affect the offspring's externalizing behavior indirectly by shaping the environment--in particular, by shaping the parent-child relationship in adolescence.



<u>Multivariate analysis of 1.5 million people identifies genetic</u> <u>associations with traits related to self-regulation and addiction</u>

The results of this study provide insight into the genetic nature of externalizing behavior and its wide-ranging consequences. Previous studies demonstrate a genetic risk underlying all externalizing outcomes (e.g. substance abuse, disruptive behavioral problems) but no effort at a large-scale gene identification had previously been made. In this paper, scientists looked at genetic data from ~1.5 million people and identified 579 areas associated with a general tendency towards externalizing. These genes were also correlated specifically with substance use and abuse.

#### <u>Comparison of Parent, Peer, Psychiatric, and Cannabis Use Influences Across Stages of Offspring Alcohol</u> <u>Involvement: Evidence from the COGA Prospective Study</u>

Alcohol use disorder develops in stages–from first use, to first alcohol-related problem, to experiencing enough symptoms to qualify for an alcohol use disorder. This study looked at factors that might increase or decrease the chance of acquiring the disorder. The authors considered alcohol use by parents and friends, separation from a parent, household income, history of trauma, and drug use, as well as internalizing and externalizing behaviors. The researchers found that marijuana use and externalizing behaviors had the most significant effect on increasing the rate of developing alcoholism, although some of the other factors were involved as well.