Genotype-Phenotype feasibility studies on khat abuse, traumatic experiences and psychosis in Ethiopia

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INTRODUCTION
Khat trees are native to East Africa and the Arabian Peninsula; their leaves contain amphetamine-like alkaloids such as cathinone, cathine, and norpseudoephedrine and are chewed for their stimulating and euphoric effects. Chewing khat has a long tradition among some ethnic groups but due to increased crop cultivation it has spread further among the male population. Khat use varies by season: in the dry season there is limited availability and market prices are high; in the rainy season, the opposite is true. Typical patterns of consumption range from moderate to problematic. Excessive use is associated with dependence and khat-induced psychosis.

PILOT STUDY
Environmental factors are considered important factors in the etiopathogenesis of psychosis. In a pilot study we reported on the environmental factors khat use and traumatic experiences and their association with psychotic symptoms in the general population of Southwestern Ethiopia. (Adorjan K. J. et al. Schulze TG: Khat use and occurrence of psychotic symptoms in the general male population in Southwestern Ethiopia: evidence for sensitization by traumatic experiences, World Psychiatry, October 2017).

In collaboration with the Gilgel Gibe Field Research Center of Jimma University, we studied khat use and khat-induced psychotic symptoms in a survey of 1,100 men aged 18 to 40 years (M 28.4; SD 6.6), selected from the center’s population registry by stratified (rural, urban) cluster random sampling. Initial participation rate was 79.1%. Total population is 60,000, an estimated 63% of men use khat.

RESULTS - GENOTYPE
The genotyping of all individuals in the genetic pilot study was successfully completed with high quality. The overall sample call rate after genotyping was 99.21%. We followed standard quality control (QC) protocols to process our data including parameters such as call rate, deviations from HWE, minor allele frequency (MAF) and others. A total of around 2.54% of the SNPs (17,765 SNPs) were removed due to low call rate (98%), 1.67% of SNPs (11,401 SNPs) were removed due to deviations from HWE, and 42.19% (283,074 SNPs) showed a MAF < 1%. Please note that a sample size of only 100 individuals doesn’t allow for a precise estimation of MAF in this sample cohort. One person needed to be excluded due to low call rate (98%) and an additional 3 individuals were removed to due relatedness within the sample (pi-hat > 0.2 after additional QC and LD pruning following standard protocols). We found no signs of sample contamination (based on inbreeding coefficients).

After QC we subjected our sample to principle component analysis (PCA) to identify potential sample heterogeneity. Furthermore, we were interested to map our cohort in comparison to the African samples that have been part of the 1000 Genomes project. For this purpose we merged our data with the 1000 genomes data for the African populations (661 rest to map our cohort in comparison to the African samples that have been part of the 1000 Genomes project. For this purpose we merged our data with the 1000 genomes data for the African populations (661 samples in total). Figure 1 shows the result of this analysis. As expected, initial GWAS (using a linear regression with PCA covariates 1-4) of the norephedrine concentration in urine in the genotyped samples (n=387,836) did not reveal any reliable association (data not shown). Next steps will include imputation of our study samples using markers (n=387,836) did not reveal any reliable association (data not shown).

CONCLUSION
Encouraged by the results of our pilot studies we are currently preparing the full study of a sample size of 10,000 to study genetic variation and gene-environment interactions in Ethiopia, especially the relationship of khat abuse and the development of psychotic symptoms and its interactions with genetic factors. The GERP is a unique opportunity to build well-characterized cohorts of individuals and to perform genetic studies that so far have not been undertaken in Ethiopia. This study will complement other efforts currently underway in Africa. Moreover, we will be in the unique position to study the relationship of khat use, psychosis and trauma. The information obtained by this pilot study on DNA is instrumental for the preparation of a comprehensive genetic study in a developing country.