

## Genome-Wide Association Study of Hoarding Traits

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### TO THE EDITOR

Hoarding is characterized by difficulty discarding or parting with possessions, resulting in clutter that impedes the normal use of living spaces [Frost and Hartl, 1996]. Although hoarding can be a symptom of multiple neurological and psychiatric disorders, such as obsessive-compulsive disorder (OCD), mounting evidence suggests that once other primary causes are ruled out, hoarding can also be a discrete disorder [Mataix-Cols et al., 2010]. The DSM-V taskforce is currently considering the creation of a new diagnostic category named hoarding disorder ([www.dsm5.org](http://www.dsm5.org)). We have recently shown that hoarding is highly prevalent and heritable, with genetic factors accounting for approximately 50% of its variance [Iervolino et al., 2009]. Very few studies have examined the genetic architecture of hoarding, and their results have been largely inconsistent [Zhang et al., 2002; Samuels et al., 2007; Pertusa et al., 2010].

We conducted a genome-wide association study for hoarding traits in a large cohort of Caucasian twins (see [Iervolino et al., 2009] for more details). A sub-sample of 3,410 participants had been genotyped and was included in this study. Of these participants, 2,350 were singletons (either MZ as MZ twins are genetically identical, only one member of the twin pair was genotyped- or DZ without the co-twin), predominantly female (91.8%), with a mean age of 56.8 years (SD = 12.6; range = 17–85). All participants completed the Hoarding Rating Scale-Self-Report (HRS-SR [Tolin et al., 2010]), a brief self-administered instrument consisting of five items (clutter, difficulty discarding, excessive acquisition, distress, and impairment). Each item is scored from 0 (none) to 8 (extreme) with a total score ranging from 0 to 40. Scores above 14 indicate severe hoarding with sensitivity and specificity of 0.97. HRS scores were obtained for each member of a MZ twin pair but only one twin was genotyped. In order to minimize measurement error and get a better estimate, the HRS-SR scores of each MZ twin pair were treated as biological duplicates and averaged. The mean HRS-SR score in our cohort was of 2.83 (SD = 4.2; range = 0–35).

Subjects were genotyped using either Illumina 317 K (n = 1,348) or 610 K (n = 2,062) BeadChips. All subsequent analyses were

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carried out using PLINK software [Purcell et al., 2007]. After quality control procedure and imputation of genotypes (Supplementary Information), a dataset composed of 3,304 individuals and 1,517,033 SNPs was available for analyses.

A HRS-SR score adjusted by age and the first two principal components of the population stratification analysis was used for association. To account for the dependence between related individuals, we used the `-qfam-total` option with permutations designed to extract all association information from a family-based sample [Purcell et al., 2007]. The `-qfam` procedure adopts the between/within model and performs a simple linear regression of phenotype on genotype using a special permutation procedure to correct for family structure allowing to integrate both singletons and related individuals in a same analysis. Finally, the inflation coefficient factor after permutation was of 0.98 suggesting no inflation of the tests statistics.

Although no SNP demonstrated evidence for association at a genome-wide level of significance, two genomic loci on

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chromosome 5 and 6 showed suggestive evidence for association with hoarding traits. Five high-correlated SNPs encompassing the 5' end of the gene for the Leber Congenital Amaurosis 5 (*LCA5*) on chromosome 6q14.1 showed  $P$ -values ranging from  $4.36 \times 10^{-5}$  to  $7 \times 10^{-7}$  (Fig. 1 and Supplementary Table S1). The most significant SNP was rs3747767. The mean HRS-SR score was 2.75 (SD = 3.9) for AA subjects (N = 3,060), 4.57 (SD = 6.8) for AC carriers (N = 162), and 6.17 (SD = 4.2) for CC carriers (N = 3). Our data suggest that a rare haplotype encompassing the 5' end of the *LCA5* gene may confer increased susceptibility for hoarding traits. Mutations of the *LCA5* gene, which encodes the ubiquitous ciliary protein lebercilin, cause Leber Congenital Amaurosis, a form of severe visual impairment that has also been associated with neurological abnormalities, albeit inconsistently [den Hollander et al., 2008].

Eight common SNPs on chromosome 5, in high LD ( $r^2 > 0.9$ ) with each other, also showed suggestive evidence for association with hoarding traits (Fig. 1 and Supplementary Table S1). These SNPs are located in a "gene desert" region of approximately 1 Mb on chromosome 5q11.2 and are flanking a common copy number variant (<http://projects.tcag.ca/cgi-bin/variation/tbrowse?source=hg18&table=Locus&num=50&rstart=504>).

Importantly, all these association signals remained at the same level of significance after adjustment for OCD traits (scores on the

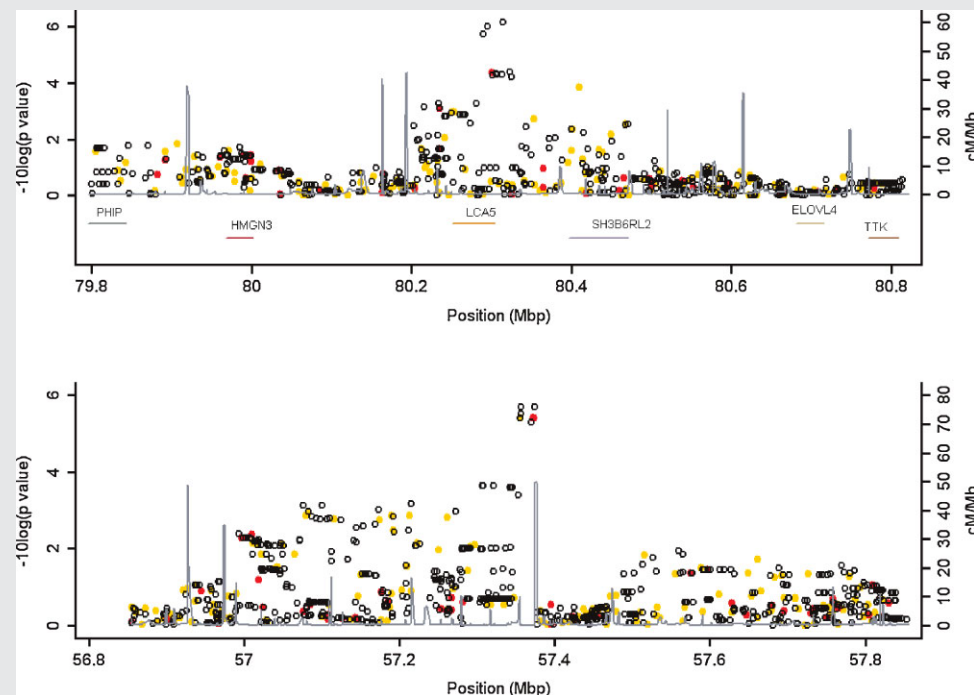
Obsessive-Compulsive Inventory-Revised; OCI-R [Foa et al., 2002]), which suggests a specific effect of these SNPs on hoarding traits over and above OCD symptoms.

The main limitations of this study are the predominance of females and the use of a self-report measure to assess hoarding. However, the HRS-SR correlates strongly with the interview version of the instrument [Tolin et al., 2010], and both versions have excellent psychometric properties and correlate highly with other measures of hoarding [Tolin et al., 2010]. Unfortunately, we were unable to perform any sex-specific analysis given the very low number of male participants in our sample ( $n = 272$ ).

Although we did not replicate the findings from previous genetic studies [Zhang et al., 2002; Samuels et al., 2007], it is important to note that this is the first genome-wide study of hoarding traits carried out in a sample of individuals who were not specifically selected for having a diagnosis of OCD or Tourette's Syndrome. Further studies involving large samples of individuals diagnosed with hoarding disorder are needed to corroborate the involvement of these regions.

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**FIG. 1.** Genome-wide analysis. Genotyped (full circles) and imputed (hollow circles) SNPs plotted by position on chromosome 6 (upper panel) and chromosome 5 (lower panel) against association with hoarding traits ( $-\log_{10} P$ -value). The panel shows 500 kb upstream and downstream of the best SNPs on chromosome 6 (upper panel) and chromosome 5 (lower panel), respectively. Estimated recombination rates (cM/Mb) (from HapMap) are plotted in gray to describe the local LD structure. Genotyped SNPs are color-coded to reflect their provenance from either both datasets (317 K and 610 K BeadChips in yellow) or only the 610 K BeadChip (red).

## REFERENCES

- den Hollander A, Roepman R, Koenekoop R, Cremers F. 2008. Leber congenital amaurosis: Genes, proteins and disease mechanisms. *Prog Retinal Eye Res* 27:391–419.
- Foa EB, Huppert JD, Leiberg S, Langner R, Kichic R, Hajcak G, Salkovskis PM. 2002. The Obsessive-Compulsive Inventory: Development and validation of a short version. *Psychol Assess* 14:485–496.
- Frost RO, Hartl TL. 1996. A cognitive-behavioral model of compulsive hoarding. *Behav Res Ther* 34:341–350.
- Iervolino AC, Perroud N, Fullana MA, Guipponi M, Cherkas L, Collier DA, Mataix-Cols D. 2009. Prevalence and heritability of compulsive hoarding: A twin study. *Am J Psychiatry* 166:1156–1161.
- Mataix-Cols D, Frost RO, Pertusa A, Clark LA, Saxena S, Leckman JF, Stein DJ, Matsunaga H, Wilhelm S. 2010. Hoarding disorder: A new diagnosis for DSM-V? *Depress Anxiety* 27:556–572.
- Pertusa A, Frost RO, Fullana MA, Samuels J, Steketee G, Tolin D, Saxena S, Leckman JF, Mataix-Cols D. 2010. Refining the diagnostic boundaries of compulsive hoarding: A critical review. *Clin Psychol Rev* 30:371–386.
- Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D, Maller J, Sklar P, de Bakker PI, Daly MJ, et al. 2007. PLINK: A tool set for whole-genome association and population-based linkage analyses. *Am J Hum Genet* 81:559–575.
- Samuels J, Shugart YY, Grados MA, Willour VL, Bienvenu OJ, Greenberg BD, Knowles JA, McCracken JT, Rauch SL, Murphy DL, et al. 2007. Significant linkage to compulsive hoarding on chromosome 14 in families with obsessive-compulsive disorder: Results from the OCD Collaborative Genetics Study. *Am J Psychiatry* 164:493–499.
- Tolin DF, Frost RO, Steketee G. 2010. A brief interview for assessing compulsive hoarding: The Hoarding Rating Scale-Interview. *Psychiatry Res*. 178:147–152.
- Zhang H, Leckman JF, Pauls DL, Tsai CP, Kidd KK, Campos MR. 2002. Genomewide scan of hoarding in sib pairs in which both sibs have Gilles de la Tourette syndrome. *Am J Hum Genet* 70:896–904.