

1 **Title: Genome-wide association analyses of risk tolerance and risky behaviors**
2 **in over 1 million individuals identify hundreds of loci and shared genetic**
3 **influences¹**

4 All authors and their affiliations are listed at the end of the manuscript.

6 **Abstract:**

7 Humans vary substantially in their willingness to take risks. In a combined sample of over one
8 million individuals, we conducted genome-wide association studies (GWAS) of general risk
9 tolerance, adventurousness, and risky behaviors in the driving, drinking, smoking, and sexual
10 domains. We identified 611 approximately independent genetic loci associated with at least one
11 of our phenotypes, including 124 with general risk tolerance. We report evidence of substantial
12 shared genetic influences across general risk tolerance and risky behaviors: 72 of the 124 general
13 risk tolerance loci contain a lead SNP for at least one of our other GWAS, and general risk
14 tolerance is moderately to strongly genetically correlated ($|\hat{r}_g| \sim 0.25$ to 0.50) with a range of
15 risky behaviors. Bioinformatics analyses imply that genes near general-risk-tolerance-associated
16 SNPs are highly expressed in brain tissues and point to a role for glutamatergic and GABAergic
17 neurotransmission. We find no evidence of enrichment for genes previously hypothesized to
18 relate to risk tolerance.

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¹ Previous title: Genome-wide study identifies 611 loci associated with risk tolerance and risky behaviors.

21 **Main Text:**

22 Choices in important domains of life, including health, fertility, finance, employment, and social
23 relationships, rarely have consequences that can be anticipated perfectly. The degree of
24 variability in possible outcomes is called risk. Risk tolerance—defined as the willingness to take
25 risks, typically to obtain some reward—varies substantially across humans and has been actively
26 studied in the behavioral and social sciences. An individual’s risk tolerance may vary across
27 domains, but survey-based measures of *general* risk tolerance (e.g., “Would you describe
28 yourself as someone who takes risks?”) have been found to be good all-around predictors of
29 risky behaviors such as portfolio allocation, occupational choice, smoking, drinking alcohol, and
30 starting one’s own business^{1–3}.

31 Twin studies have established that various measures of risk tolerance are moderately heritable
32 ($h^2 \sim 30\%$, although estimates in the literature vary^{3–5}). Discovery of specific genetic variants
33 associated with general risk tolerance could advance our understanding of how genetic
34 influences are amplified and dampened by environmental factors; provide insights into
35 underlying biological pathways; enable the construction of polygenic scores (indexes of many
36 genetic variants) that can be used as overall measures of genetic influences on individuals; and
37 help distinguish genetic variation associated with general versus domain-specific risk tolerance.

38 Although risk tolerance has been one of the most studied phenotypes in social science genetics,
39 most claims of positive findings have been based on small-sample candidate gene studies
40 (**Supplementary Table 11.1**), whose limitations are now appreciated⁶. To date, only two loci
41 associated with risk tolerance have been identified in genome-wide association studies
42 (GWAS)^{7,8}.

43 Here, we report results from large-scale GWAS of self-reported general risk tolerance (our
44 primary phenotype) and six supplementary phenotypes: “adventurousness” (defined as the self-
45 reported tendency to be adventurous vs. cautious); four risky behaviors: “automobile speeding
46 propensity” (the tendency to drive faster than the speed limit), “drinks per week” (the average
47 number of alcoholic drinks consumed per week), “ever smoker” (whether one has ever been a
48 smoker), and “number of sexual partners” (the lifetime number of sexual partners); and the first
49 principal component (PC) of these four risky behaviors, which we interpret as capturing the
50 general tendency to take risks across domains. All seven phenotypes are coded such that higher

51 phenotype values are associated with higher risk tolerance or risk taking. **Table 1** lists, for each
52 GWAS, the datasets we analyzed and the GWAS sample size.

53

54 Association analyses

55 All seven GWAS were performed in European-ancestry subjects, following procedures described
56 in a pre-specified analysis plan (<https://osf.io/cjx9m/>) and in **Supplementary Information**
57 **section 2**.

58 In the discovery phase of our GWAS of general risk tolerance ($n = 939,908$), we performed a
59 sample-size-weighted meta-analysis of results from the UK Biobank (UKB, $n = 431,126$) and a
60 sample of research participants from 23andMe ($n = 508,782$). The UKB measure of general risk
61 tolerance is based on the question: “Would you describe yourself as someone who takes risks?
62 Yes / No.” The 23andMe measure is based on a question about overall comfort taking risks, with
63 five response options ranging from “very comfortable” to “very uncomfortable.” The genetic
64 correlation⁹ between the UKB and 23andMe cohorts ($\hat{r}_g = 0.77$, $SE = 0.02$) is smaller than one
65 but high enough to justify our approach of pooling the two cohorts¹⁰.

66 The Q-Q plot (**Extended Data Fig. 3.2a**) from the discovery GWAS exhibits substantial
67 inflation ($\lambda_{GC} = 1.41$). According to the estimated intercept from a linkage disequilibrium (LD)
68 Score regression¹¹, only a small share of this inflation (~5%) in test statistics is due to bias. To
69 account for this bias, we inflated GWAS standard errors by the square root of the LD Score
70 regression intercept.

71 We identified 124 approximately independent SNPs (pairwise $r^2 < 0.1$) that attained genome-
72 wide significance ($P < 5 \times 10^{-8}$). These 124 “lead SNPs” are listed in **Supplementary Table 3.1**
73 and shown in **Fig. 1a**. All have coefficients of determination (R^2 's) below 0.02%, and the SNP
74 with the largest per-allele effect is estimated to increase general risk tolerance by ~0.026
75 standard deviations in our discovery sample (**Extended Data Fig. 3.3**).

76 In the replication phase of our GWAS of general risk tolerance (combined $n = 35,445$), we meta-
77 analyzed summary statistics from ten smaller cohorts. Additional details on cohort-level
78 phenotype measures are provided in **Supplementary Table 1.2**. The questions differ in terms of
79 their exact wording and number of response categories, but all questions ask subjects about their

80 overall or general attitudes toward risk. The genetic correlation⁹ between the discovery and
81 replication GWAS is 0.83 ($SE = 0.13$). 123 of the 124 lead SNPs were available or well proxied
82 by an available SNP in the replication GWAS results. Out of the 123 SNPs, 94 have a
83 concordant sign ($P = 1.7 \times 10^{-9}$) and 23 are significant at the 5% level in one-tailed t tests ($P =$
84 4.5×10^{-8}) (**Extended Data Fig. 5.1**). This empirical replication record matches theoretical
85 projections that take into account sampling variation and the winner's curse (**Supplementary**
86 **Information section 5**).

87 Our six supplementary GWAS—of adventurousness, four risky behaviors, and their principal
88 component ($n = 315,894$ to $557,923$; **Supplementary Tables 1.1-1.2**)—were conducted using
89 methods comparable to those in the primary GWAS, but without a replication phase. **Extended**
90 **Data Fig. 3.2 (c to h)** shows Q-Q plots and **Extended Data Fig. 3.1 (a to f)** shows Manhattan
91 plots.

92 **Table 1** provides a summary overview of the seven GWAS. We identified a total of 865 lead
93 SNPs across the seven GWAS. The lead SNPs are located in 611 approximately independent
94 loci, where a locus is defined as the set of all SNPs in weak LD (pairwise $r^2 > 0.1$) with a lead
95 SNP. The SNP heritabilities of the seven phenotypes range from ~ 0.05 (for general risk
96 tolerance) to ~ 0.16 (for the first PC of the four risky behaviors).

97

98 Genetic overlap

99 There is substantial overlap across the results of our GWAS. For example, 72 of the 124 general-
100 risk-tolerance lead SNPs are in loci that also contain lead SNPs for at least one of the other
101 GWAS, including 45 for adventurousness and 49 for at least one of the four risky behaviors or
102 their first PC. To empirically assess if this overlap could be attributed to chance, we conducted a
103 resampling exercise under the null hypothesis that the lead SNPs of our supplementary GWAS
104 are distributed independently of the 124 general-risk-tolerance lead loci. We strongly rejected
105 this null hypothesis ($P < 0.0001$; **Supplementary Information section 3.3.3**).

106 Several regions of the genome stand out for being associated both with general risk tolerance and
107 with all or most of the supplementary phenotypes. We tested whether the signs of the lead SNPs
108 located in these regions tend to be concordant across our primary and supplementary GWAS. We

109 strongly rejected the null hypothesis of no concordance ($P < 3 \times 10^{-30}$; **Supplementary**
110 **Information section 3.2.3**), suggesting that these regions represent shared genetic influences,
111 rather than colocalization of causal SNPs. **Fig. 1b** and **Extended Data Fig. 3.4** show local
112 Manhattan plots for some of these regions. The long-range LD region¹² on chromosome 3 (~83.4
113 to 86.9 Mb) contains lead SNPs from all seven GWAS as well as the most significant lead SNP
114 from the general risk tolerance GWAS, rs993137 ($P = 2.14 \times 10^{-40}$), which is located in the gene
115 *CADM2*. Another long-range LD region, on chromosome 6 (~25.3 to 33.4 Mb), covers the HLA-
116 complex and contains lead SNPs from all GWAS except drinks per week. Three candidate
117 inversions (i.e., genomic regions that are highly prone to inversion polymorphisms;
118 **Supplementary Information section 2.9.2**) on chromosomes 7 (~124.6 to 132.7 Mb), 8 (~7.89
119 to 11.8 Mb), and 18 (~49.1 to 55.5 Mb) contain lead SNPs from six, five, and all seven of our
120 GWAS, respectively. Finally, four other LD blocks¹³ that do not overlap known long-range LD
121 or candidate inversion regions each contain lead SNPs from five of our GWAS (including
122 general risk tolerance). The two long-range LD regions and the three candidate inversions have
123 previously been found to be associated with numerous phenotypes, including many cognitive and
124 neuropsychiatric phenotypes¹⁴.

125 To investigate genetic overlap at the genome-wide level, we estimated genetic correlations with
126 self-reported general risk tolerance using bivariate LD Score regression⁹. (For this and all
127 subsequent analyses involving general risk tolerance, we used the summary statistics from the
128 combined meta-analysis of our discovery and replication GWAS.) The estimated genetic
129 correlations with our six supplementary phenotypes are all positive, larger than ~0.25, and highly
130 significant ($P < 2.3 \times 10^{-30}$; **Fig. 2**), indicating that SNPs associated with higher general risk
131 tolerance also tend to be associated with riskier behavior. The largest estimated genetic
132 correlations are with adventurousness ($\hat{r}_g = 0.83$, $SE = 0.01$), number of sexual partners (0.52, SE
133 = 0.02), automobile speeding propensity (0.45, $SE = 0.02$), and the first PC of the four risky
134 behaviors (0.50, $SE = 0.02$).

135 Our estimates of the genetic correlations between general risk tolerance and the supplementary
136 risky behaviors are substantially higher than the corresponding phenotypic correlations
137 (**Supplementary Tables 1.3** and **7.1**). Although measurement error partly accounts for the low
138 phenotypic correlations, the genetic correlations remain considerably higher even after

139 adjustment of the phenotypic correlations for measurement error. The comparatively large
140 genetic correlations support the view that a general factor of risk tolerance partly accounts for
141 cross-domain variation in risky behavior^{15,16} and imply that this factor is genetically influenced.
142 The lower phenotypic correlations suggest that environmental factors are more important
143 contributors to domain-specific risky behavior^{17,18}.

144 To increase the precision of our estimates of the SNPs' effects on general risk tolerance, we
145 leveraged the high degree of genetic overlap across our phenotypes by conducting Multi-Trait
146 Analysis of GWAS (MTAG)¹⁹. We used as inputs the summary statistics of our GWAS of
147 general risk tolerance, of our first five supplementary GWAS (i.e., not including the first PC of
148 the four risky behaviors), and of a previously published GWAS on lifetime cannabis use²⁰
149 (**Supplementary Information section 9**). MTAG increased the number of general-risk-tolerance
150 lead SNPs from 124 to 312 (**Extended Data Fig. 9.1, Supplementary Table 9.1**).

151 We also estimated genetic correlations between general risk tolerance and 28 additional
152 phenotypes (**Fig. 2** and in **Supplementary Table 7.1**). These included phenotypes for which we
153 could obtain summary statistics from previous GWAS, as well as five phenotypes for which we
154 conducted new GWAS. The estimated genetic correlations for the personality traits extraversion
155 ($\hat{r}_g = 0.51$, $SE = 0.03$), neuroticism (-0.42 , $SE = 0.04$), and openness to experience (0.33 , $SE =$
156 0.03) are substantially larger in magnitude than previously reported phenotypic correlations²¹,
157 pointing to substantial shared genetic influences among general risk tolerance and these traits.
158 After Bonferroni correction, we also find significant positive genetic correlations with the
159 neuropsychiatric phenotypes ADHD, bipolar disorder, and schizophrenia. Viewed in light of the
160 genetic correlations we find with risky behaviors classified as externalizing (e.g., substance use,
161 elevated sexual behavior, and fast driving), these results suggest the hypothesis that the overlap
162 with the neuropsychiatric phenotypes is driven by their externalizing component.

163

164 Biological annotation

165 To gain insights into the biological mechanisms through which genetic variation influences
166 general risk tolerance, we conducted a number of analyses. First, we systematically reviewed the
167 literature that aimed to link risk tolerance to biological pathways (**Supplementary Information**
168 **section 11**). Our review covered studies based on candidate genes (i.e., specific genetic variants

169 used as proxies for biological pathways), pharmacological manipulations, biochemical assays,
170 genetic manipulations in rodents, as well as other research designs. Our review identified 132
171 articles that matched our search criteria (**Supplementary Table 11.1**).

172 Previous work has focused on five main biological pathways: the steroid hormone cortisol, the
173 monoamines dopamine and serotonin, and the steroid sex hormones estrogen and testosterone.
174 Using a MAGMA²² competitive gene-set analysis, we found no evidence that SNPs within genes
175 associated with these five pathways tend to be more associated with general risk tolerance than
176 SNPs in other genes (**Supplementary Table 11.3**). Further, none of the other bioinformatics
177 analyses we report below point to these pathways.

178 We also examined the 15 most commonly tested autosomal genes within the dopamine and
179 serotonin pathways, which were the focus of most of the 34 candidate-gene studies identified by
180 our literature review. We verified that the SNPs available in our GWAS results tag most of the
181 genetic variants typically used to test the 15 genes. Across one SNP-based test and two gene-
182 based tests, we found no evidence of non-negligible associations between those genes and
183 general risk tolerance (**Fig. 1c** and **Supplementary Table 11.4**). (We note, however, that some
184 brain regions identified in analyses we report below are areas where dopamine and serotonin
185 play important roles.)

186 Second, we performed a MAGMA²² gene analysis to test each of ~18,000 protein-coding genes
187 for association with general risk tolerance (**Supplementary Information section 12.2**). After
188 Bonferroni correction, 285 genes were significant (**Extended Data Fig. 12.1** and
189 **Supplementary Table 12.3**). To gain insight into the functions and expression patterns of these
190 285 genes, we looked up these genes in the Gene Network²³ co-expression database. Third, to
191 identify relevant biological pathways and identify tissues in which genes near general-risk-
192 tolerance-associated SNPs are expressed, we applied the software tool DEPICT²⁴ to the SNPs
193 with P values less than 10^{-5} in our GWAS of general risk tolerance (**Supplementary**
194 **Information section 12.4**).

195 Both the Gene Network and the DEPICT analyses separately point to a role for glutamate and
196 GABA neurotransmitters, which are the main excitatory and inhibitory neurotransmitters in the
197 brain, respectively²⁵ (**Fig. 3a** and **Supplementary Tables 12.4** and **12.8**). To our knowledge, no
198 published large-scale GWAS of cognition, personality, or neuropsychiatric phenotypes has

199 pointed to clear roles both for glutamate and GABA (although glutamatergic neurotransmission
200 has been implicated in recent GWAS of schizophrenia²⁶ and major depression²⁷). Our results
201 suggest that the balance between excitatory and inhibitory neurotransmission may contribute to
202 variation in general risk tolerance across individuals.

203 The Gene Network and the DEPICT tissue enrichment analyses also both separately point to
204 enrichment of the prefrontal cortex and the basal ganglia (**Fig. 3b** and **Supplementary Tables**
205 **12.4, 12.6, and 12.7**). The cortical and subcortical regions highlighted by DEPICT include some
206 of the major components of the cortical-basal ganglia circuit, which is known as the reward
207 system in human and non-human primates and is critically involved in learning, motivation, and
208 decision-making, notably under risk and uncertainty^{28,29}. We caution, however, that our results
209 do not point exclusively to the reward system.

210 Lastly, we used stratified LD Score regression³⁰ to test for the enrichment of SNPs associated
211 with histone marks in 10 tissue or cell types (**Supplementary Information section 12.1**).
212 Central nervous system tissues are the most enriched, accounting for 44% ($SE = 3\%$) of the
213 heritability while comprising only 15% of the SNPs (**Extended Data Fig. 12.3a** and
214 **Supplementary Table 12.2**). Immune/hematopoietic tissues are also significantly enriched.
215 While a role for the immune system in modulating risk tolerance is plausible given prior
216 evidence of its involvement in several neuropsychiatric disorders^{26,27}, future work is needed to
217 confirm this result and to uncover specific pathways that might be involved.

218

219 Polygenic prediction

220 We constructed polygenic scores of general risk tolerance to gauge their potential usefulness in
221 empirical research (**Supplementary Information section 10**). We used the Add Health, HRS,
222 NTR, STR, UKB-siblings, and Zurich cohorts as validation cohorts (**Supplementary Table 1.1**
223 provides an overview of these cohorts; the UKB-siblings cohort comprised individuals with at
224 least one full sibling in the UKB). For each validation cohort, we constructed the score using
225 summary statistics from a meta-analysis of our discovery and replication GWAS that excluded
226 the cohort. Our measure of predictive power is the incremental R^2 (or pseudo- R^2) from adding
227 the score to a regression of the phenotype on sex, birth year, and the top ten principal
228 components of the genetic relatedness matrix.

229 Our preferred score was constructed with LDpred³¹. In the UKB-siblings cohort, which is our
230 largest validation cohort ($n \sim 35,000$), the score's predictive power is 1.6% for general risk
231 tolerance, 1.0% for the first PC of the four risky behaviors, 0.8% for number of sexual partners,
232 0.6% for automobile speeding propensity, and $\sim 0.15\%$ for drinks per week and ever smoker.
233 Across our validation cohorts, the score is also predictive of several personality phenotypes and a
234 suite of real-world measures of risky behaviors in the health, financial, career, and other domains
235 (**Extended Data Figs. 10.1-10.2** and **Supplementary Tables 10.1-10.3**). The incremental R^2 we
236 observe for general risk tolerance is consistent with the theoretical prediction, given the SNP
237 heritability of general risk tolerance (**Table 1**) and the imperfect genetic correlations across the
238 GWAS and validation cohorts^{32,33} (**Supplementary Information section 10.4**).

239

240 Discussion

241 Our results provide insights into biological mechanisms that influence general risk tolerance. Our
242 bioinformatics analyses point to the role of gene expression in brain regions that have been
243 identified by neuroscientific studies on decision-making, notably the prefrontal cortex, basal
244 ganglia, and midbrain, thereby providing convergent evidence with that from neuroscience^{28,29}.
245 Yet our analyses failed to find evidence for the main biological pathways that had been
246 previously hypothesized to influence risk tolerance. Instead, our analyses implicate genes
247 involved in glutamatergic and GABAergic neurotransmission, which were heretofore not
248 generally believed to play a role in risk tolerance.

249 Although our focus has been on the genetics of general risk tolerance and risky behaviors,
250 environmental and demographic factors account for a substantial share of these phenotypes'
251 variation. We observe sizeable effects of sex and age on general risk tolerance in the UKB data
252 (**Extended Data Fig. 1.1**), and life experiences have been shown to affect both measured risk
253 tolerance and risky behaviors (e.g., refs. 34,35). The data we have generated will allow
254 researchers to construct and use polygenic scores of general risk tolerance to measure how
255 environmental, demographic, and genetic factors interact with one another.

256 For the behavioral sciences, our results bear on the ongoing debate about the extent to which risk
257 tolerance is a "domain-general" as opposed to a "domain-specific" trait. Low phenotypic
258 correlations in risk tolerance across decision-making domains have been interpreted as

259 supporting the domain-specific view^{17,18}. Across the risky behaviors we study, we find that the
260 genetic correlations are considerably higher than the phenotypic correlations (even after the latter
261 are corrected for measurement error) and that many lead SNPs are shared across our phenotypes.
262 These observations suggest that the low phenotypic correlations across domains are due to
263 environmental factors that dilute the effects of a genetically-influenced domain-general factor of
264 risk tolerance.

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- 349
- 350

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363 **Information section 13**.

364

365 **Author Contributions** A full list of author contributions is included in **Supplementary**
366 **Information section 13**.

367

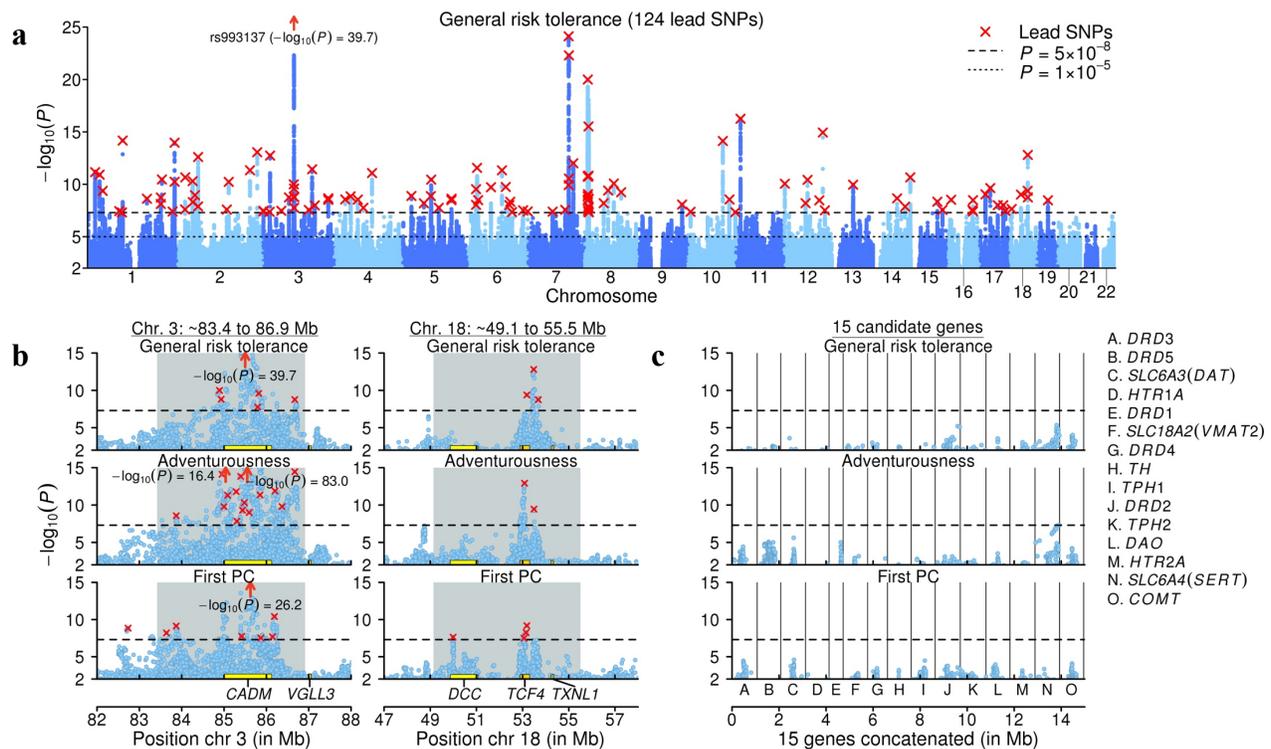
368 **Author Information** Adam Auton, Pierre Fontanillas, David A Hinds, and Aaron Kleinman are
369 employees of 23andMe, and Ronald Kessler has had ties to various companies in the past three
370 years; the authors declare no other competing financial interests. Further details are provided in
371 **Supplementary Information section 13**. Correspondence and requests for materials should be
372 addressed to J.P.B. (jonathan.pierre.beauchamp@gmail.com), R.K.L. (r.karlssonlinner@vu.nl).

373

374 **Data Availability** Upon publication, results can be downloaded from the SSGAC website
375 (<http://thessgac.org/data>).

376

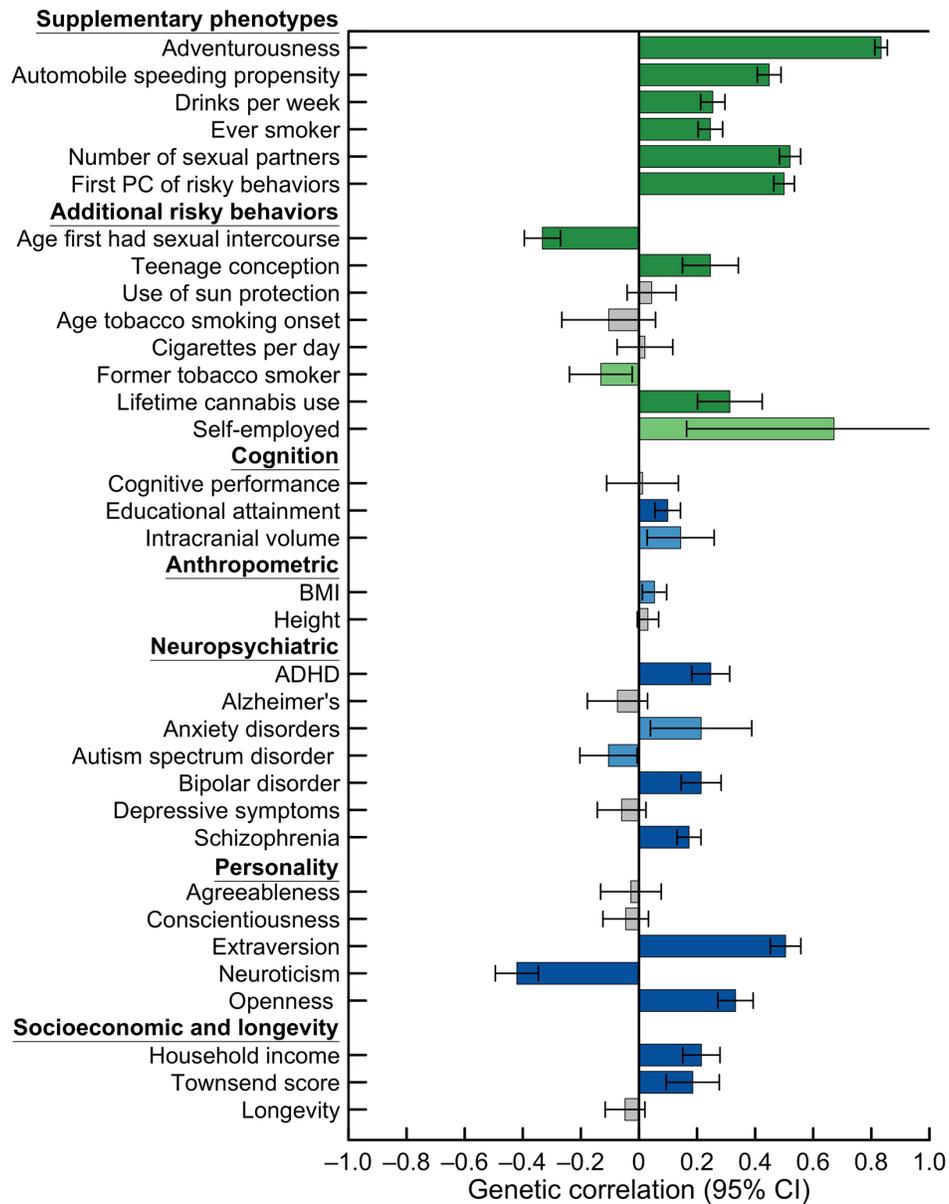
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378 **Figure 1 | Manhattan plots.** In all panels, the x-axis is chromosomal position; the y-axis is the
 379 significance on a $-\log_{10}$ scale; the horizontal dashed line marks the threshold for genome-wide
 380 significance ($P = 5 \times 10^{-8}$); and each approximately independent (pairwise $r^2 < 0.1$) genome-wide
 381 significant association (“lead SNP”) is marked by a red \times . **a**, Manhattan plots for the discovery
 382 GWAS of general risk tolerance. **b**, Local Manhattan plots of two genomic regions that contain
 383 lead SNPs for all seven of our GWAS. The gray background marks the locations of long-range
 384 LD or candidate inversion regions. **c**, Local Manhattan plots of the loci around the 15 most
 385 commonly tested candidate genes in the prior literature on the genetics of risk tolerance. Each
 386 locus comprises all SNPs within 500 kb of the gene’s borders that are in LD ($r^2 > 0.1$) with a
 387 SNP in the gene. The 15 plots are concatenated and shown together in the panel, divided by the
 388 black vertical lines. The 15 genes are not particularly strongly associated with general risk
 389 tolerance or the risky behaviors, as can be seen by comparing the results within each row across
 390 panels **b** and **c** (the three rows correspond to the GWAS of general risk tolerance,
 391 adventurousness, and the first PC of the four risky behaviors).

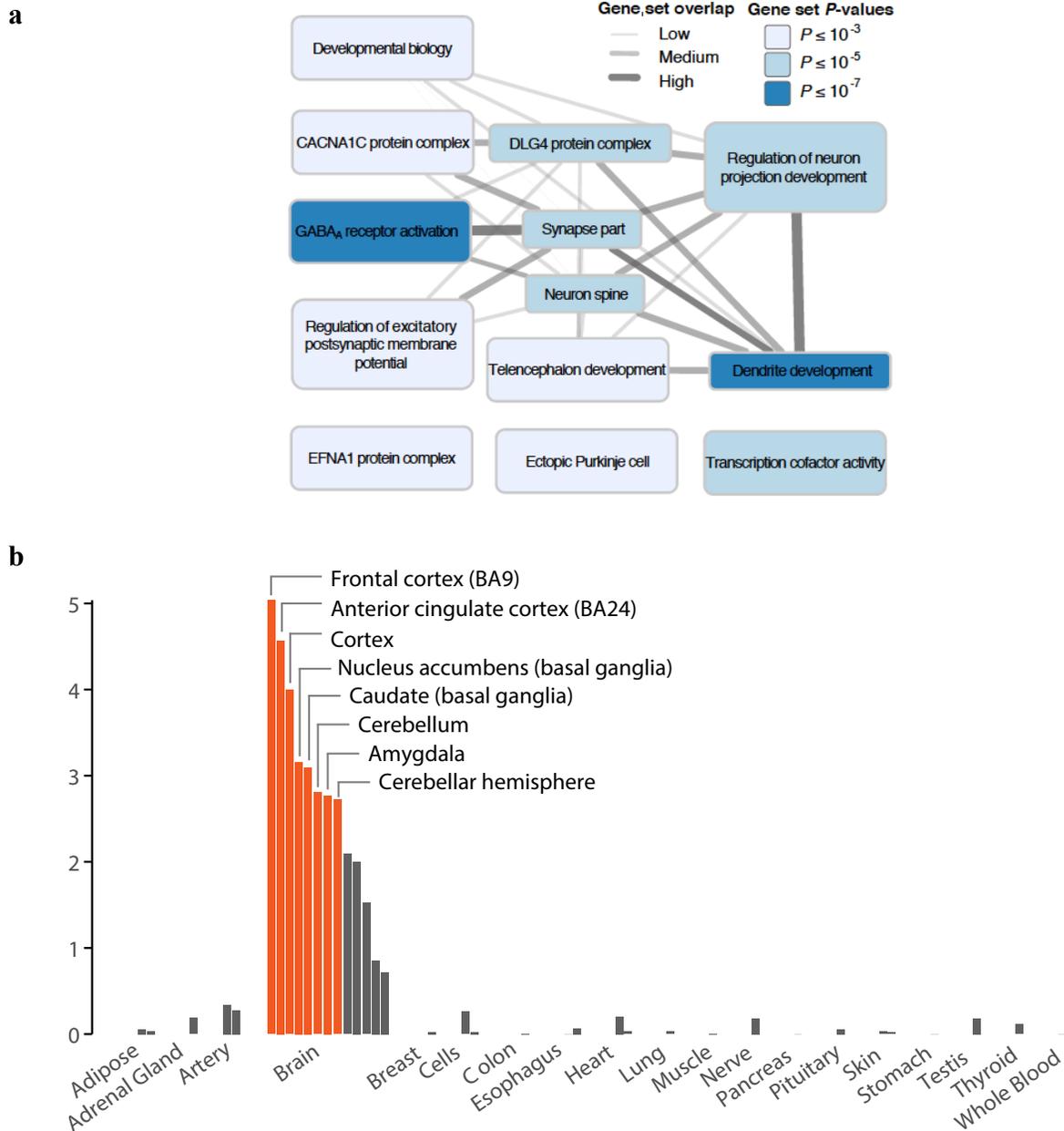
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395 **Figure 2 | Genetic correlations with general risk tolerance.** The genetic correlations were
 396 estimated using bivariate LD Score (LDSC) regression⁹. Error bars show 95% confidence
 397 intervals. For the supplementary phenotypes and the additional risky behaviors, green bars
 398 represent significant estimates with the expected signs, where higher risk tolerance is associated
 399 with riskier behavior. For the other phenotypes, blue bars represent significant estimates. Light
 400 green and light blue bars represent genetic correlations that are statistically significant at the 5%
 401 level, and dark green and dark blue bars represent correlations that are statistically significant
 402 after Bonferroni correction for 34 tests (the total number of phenotypes tested). Grey bars
 403 represent correlations that are not statistically significant at the 5% level.



404 **Figure 3 | Results from selected biological analyses. a**, DEPICT gene-set enrichment diagram.
 405 We identified 93 reconstituted gene sets that are significantly enriched ($FDR < 0.01$) for genes
 406 overlapping loci associated with general risk tolerance; using the Affinity Propagation method³⁶,
 407 these were grouped into the 13 clusters displayed in the graph. Each cluster was named after the
 408 most significant gene set it contained, and each cluster's color represents the permutation P value
 409 of its most significant gene set. The “synapse part” cluster includes the gene set “glutamate
 410 receptor activity,” and several members of the “GABA_A receptor activation” cluster are defined
 411 by gamma-aminobutyric acid signaling. Overlap between the named representatives of two

412 clusters is represented by an edge. Edge width represents the Pearson correlation ρ between the
413 two respective vectors of gene membership scores ($\rho < 0.3$, no edge; $0.3 \leq \rho < 0.5$, thin edge; 0.5
414 $\leq \rho < 0.7$, intermediate edge; $\rho \geq 0.7$, thick edge). **b**, Results of DEPICT tissue enrichment
415 analysis using GTEx data. The panel shows whether the genes overlapping loci associated with
416 general risk tolerance are significantly overexpressed (relative to genes in random sets of loci
417 matched by gene density) in various tissues. Tissues are grouped by organ or tissue type. The
418 orange bars correspond to tissues with significant overexpression (FDR < 0.01). The y-axis is the
419 significance on a $-\log_{10}$ scale.

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Table 1 | GWAS results

GWAS	Cohorts analyzed	<i>n</i>	Mean χ^2	LD Score intercept (<i>SE</i>)	# lead SNPs	SNP h^2 (<i>SE</i>)
General risk tolerance (disc. GWAS)	UKB; 23andMe	939,908	1.85	1.04 (0.01)	124	0.046 (0.001)
General risk tolerance (rep. GWAS)	10 indep. cohorts	35,445	1.03	1.00 (0.07)	0	--
General risk tolerance (disc. + rep.)	UKB; 23andMe; 10 indep. cohorts	975,353	1.87	1.04 (0.01)	132	0.045 (0.001)
Adventurousness	23andMe	557,923	1.98	1.05 (0.01)	167	0.098 (0.002)
Automobile speeding propensity	UKB	404,291	1.53	1.03 (0.01)	42	0.079 (0.003)
Drinks per week	UKB	414,343	1.61	1.03 (0.01)	85	0.085 (0.003)
Ever smoker	UKB; TAG Consortium ³⁷	518,633	1.97	1.05 (0.01)	223	0.109 (0.003)
Number of sexual partners	UKB	370,711	1.77	1.04 (0.01)	118	0.128 (0.003)
First PC of the four risky behaviors	UKB	315,894	1.77	1.05 (0.01)	106	0.156 (0.004)

The table provides an overview of the GWAS of our primary and supplementary phenotypes. “*n*”: GWAS sample size; “Mean χ^2 ”: mean GWAS chi-squared statistics across HapMap3 SNPs with minor allele frequency (MAF) greater than 0.01; “LD Score intercept”: estimate of the intercept from a LD Score regression¹¹ using HapMap3 SNPs with MAF greater than 0.01; “# lead SNPs”: number of lead SNPs, calculated after the associated statistics have been adjusted using the estimated LD score intercept; “SNP h^2 ”: SNP heritability estimated with the Heritability Estimator from Summary Statistics (HESS) method³⁸ using 1000 Genomes phase 3 SNPs with MAF greater than 0.05; “disc.”: discovery; “rep.”: replication; “indep.”: independent.

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