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Genetic Factors, Cultural Predispositions, Happiness and Gender Equality

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ABSTRACT. This paper examines correlations between the genetic characteristics of human populations and their aggregate levels of tolerance and happiness. A metadata analysis of genetic polymorphisms supports the interpretation that a major cause of the systematic clustering of genetic characteristics may be climatic con-

ditions linked with relatively high or low levels of parasite vulnerability. This led vulnerable populations to develop gene pools conducive to avoidance of strangers, while less-vulnerable populations developed gene pools linked with lower levels of avoidance. This, in turn, helped shape distinctive cultures and subsequent economic development. Survey evidence from 48 countries included in the World Values Survey suggests that a combination of cultural, economic and genetic factors has made some societies more tolerant of outsiders and more predisposed to accept gender equality than others. These relatively tolerant societies also tend to be happier, partly because tolerance creates a less stressful social environment. Though economic development tends to make all societies more tolerant and open to gender equality and even somewhat happier, these findings suggest that cross-national differences in how readily these changes are accepted, may reflect genetically-linked cultural differences.

Keywords: genetic influences; gender equality; homosexuality; tolerance; happiness; World Values Survey

1. Genetic Factors, Cultural Predispositions, Happiness and Gender Equality

Evidence that people's happiness levels are influenced by genetic factors has been growing ever since neuroscientists first discovered close linkages between happiness and dopamine and serotonin levels in the brain, and that genes seem to play a major role in regulating these levels.[1,2] An early study of over 3,000 identical and fraternal twins found that genetically identical twins reported much more similar levels of happiness even when they had different life experiences than fraternal twins.[3] If genetic factors are involved, this could help explain why given individuals tend to have relatively high or low levels of happiness. Though recent events can raise or lower these levels, in the long run, people tend to return to a baseline level of subjective well-being.[4]

Subsequent twin-based studies have found further evidence of genetic influences on happiness,[5] but twin studies do not identify which genes might be involved. Only recently has the linkage with happiness been traced to a specific gene, the serotonin transporter gene *5HTT*. Variation in the promoter region of this gene (5-HTTLPR) has been linked with personality and mental health and selective processing of positive and negative emotional stimuli.[6,7,8] And previous research suggests that the short allele is linked with depression and anxiety.[9,10,11,12] Analyzing data from 2,574 American students, De Neve found that individuals with the transcriptionally more efficient long allele of the 5-HTTLPR gene reported substantially higher levels of happiness, as measured by life satisfaction, than did individuals with the short allele.[13] Both alleles produce the same protein, but the long allele is associ-

ated with approximately three times higher basal activity than the short allele, resulting in increased gene expression and alteration of serotonin availability in the synaptic cleft for signaling. De Neve's analysis indicates that individuals with two long alleles of the 5-HTTLPR gene are about 17 percentage points likelier to report being very satisfied with their lives than those with two short alleles.

Previous studies of the linkages between genetic factors and happiness have been based on twin studies, but De Neve analyzes data from the ACT, a survey of individuals who provided DNA samples as well as questionnaire responses. This article examines data from another source: in recent years, research on the serotonin transporter gene has been carried out in many countries and the published reports provide evidence of the distribution of the respective alleles in many countries. In 48 of these countries, representative national samples of the publics were also interviewed in the World Values Survey, providing data on life satisfaction and other attitudes, together with information about each country's economic and social characteristics. Analysis of this cross-national database sheds new light on previous work, making it possible to examine the impact of societal characteristics such as the country's level of economic development or social tolerance. These factors are constants in studies carried out within any one country, making it impossible to examine their impact cannot be analyzed in single-country studies. But, as we will see, these factors vary a great deal cross-nationally and seem to have considerable impact.

Moreover, we also have data from published sources on the allele frequencies of Val158Met (rs4680) polymorphism in the catechol-O-methyltransferase (COMT) gene, and can examine its linkage with the happiness levels of the populations of 48 countries. This gene plays an important role in the inactivation of dopamine, which is linked with pro-social behavior such as empathy, cooperativeness and altruism.[14,15,16] The evidence examined here suggests that 158Met allele frequencies vary cross-nationally along with level of happiness. If differences in levels of happiness and subjective well-being are linked to genetic characteristics, then we might expect these differences to play a role in cross-national differences.

Evidence of national-level linkages does not refute findings from individual-level analysis. If two variables go together at the individual level, they usually go together at the level of large groups, but this is not necessarily true. National-level linkages can be considerably stronger or weaker than individual-levels linkages and under some circumstances they can even have opposite polarity. We repeat: national-level findings do not refute individual-level findings – but they can shed light on how individual-level genetic factors interact with societal factors, to shape a society's level of happiness. As we will see, societal-level phenomena seem to play at least

as important a role as genetic differences in shaping the happiness level of a given country's people. Moreover, the national-level linkage that we find between happiness and the Val158Met polymorphism in the COMT gene is strong enough to suggest that it merits further analysis at the individual level.

Our findings suggest that cross-national differences in happiness, tolerance of homosexuality and support for gender equality and may reflect cultural differences rooted in genetic factors. There is evidence that economic development brings tends to bring rising levels of happiness, particularly as a society rises from subsistence-level poverty to a modest level of economic security;[17] and higher levels of development tend to bring rising support for gender equality and tolerance of homosexuality.[18] Nevertheless, the speed with which given societies accept these changes may be influenced by genetically-linked cultural predispositions.

2. Findings

Twin studies have consistently found that individual differences in major personality dimensions are significantly influenced by genetic factors[19,20] but it is difficult to determine which genes are involved. Various studies have found evidence indicating that polymorphism in both the 5-HTT gene and the COMT gene are linked with differences in the Big Five Personality traits (Extraversion, Agreeableness, Conscientiousness, Neuroticism and Openness).[21,22,23,24,25,26,27]

Table 1 Correlations between national mean scores on personality variables, values and societal traits, and 5-HTTLPR and COMT 158Met allele frequencies

	Frequency of short allele of 5-HTTLPR polymorphism	**Frequency of 158Met allele of COMT gene**
Big 5: Extraversion	-.41* (32)	.38* (30)
Big 5: Agreeableness	-.61** (32)	.38* (30)
Big 5: Conscientiousness	-.55** (33)	.31 (30)
Big 5: Neuroticism	.28 (33)	-.28 (30)
Big 5: Openness	-.43* (33)	.43* (30)
Big 5: 1st principal component	-.72** (32)	.52* (30)

* significant at .05 level; ** significant at .01 level.
Number of countries is in parentheses.

Table 1 shows the correlations found between the national mean scores on the Big Five personality traits and the frequencies of the 5-HTTLPR S-allele and COMT 158Met allele in all countries for which data on both

variables are available. It also shows the linkages with the first principal component underlying the Big Five personality traits. The results support previous findings based on individual-level data, that these genes are linked with key personality traits. Both genetic polymorphisms show statistically significant linkages with several of the personality traits, and their linkages with the underlying personality dimension (on which Neuroticism shows negative loadings while the four other traits show strong positive loadings) are particularly strong, with the Val158Met polymorphism showing a .52 correlation, and the 5-HTTLPR polymorphism showing a -.72 correlation with this dimension.

Table 2 Correlations between national mean scores on personality variables values and societal traits, and Life Satisfaction

	Correlation with Life Satisfaction:
Big 5: Extraversion	.24 (51)
Big 5: Agreeableness	.01 (51)
Big 5: Conscientiousness	-.25 (51)
Big 5: Neuroticism	.14 (52)
Big 5: Openness	.18 (52)
Big 5: 1st principal component	.01 (50)
5-HTTLPR short allele frequency, %	.22 (48)
COMT 158Met allele frequency, %	.49*** (48)

* significant at .05 level; ** significant at .01 level; *** significant at .001 level
Number of countries is in parentheses.

To what extent are these personality traits linked with happiness? This analysis uses the respondent's reported satisfaction with life as a whole as an indicator of happiness or overall subjective well-being. This indicator has been validated extensively[28] and was also used by De Neve (2011) in analyzing the impact of the5-HTTLPR polymorphism on happiness. As Table 2 indicates, the Big Five personality traits are only weakly linked with life satisfaction, with none showing a statistically significant correlation. And surprisingly, the linkage of the 5-HTTLPR polymorphism with life satisfaction not only fails to reach statistical significance, but has the wrong sign. In previous individual-level research within single countries, the short allele of this gene was negatively linked with life satisfaction; but at the national level, it shows a weakly *positive* correlation – despite the fact that (as Table 1 demonstrates) it shows significant negative linkages with agree-ableness, extraversion, conscientiousness and openness, all of which would be expected to go with happiness. On the other hand, the COMT 158Met allele does show a statistically significant linkage with life satisfaction, and in the expected direction: this is logical since it is conducive to relatively

high levels of dopamine, which are linked with feelings of well-being. Moreover, in previous studies the 158Met allele has been linked with pro-social behavior, empathy and cooperativeness, which one would expect to be conducive to subjective well-being.

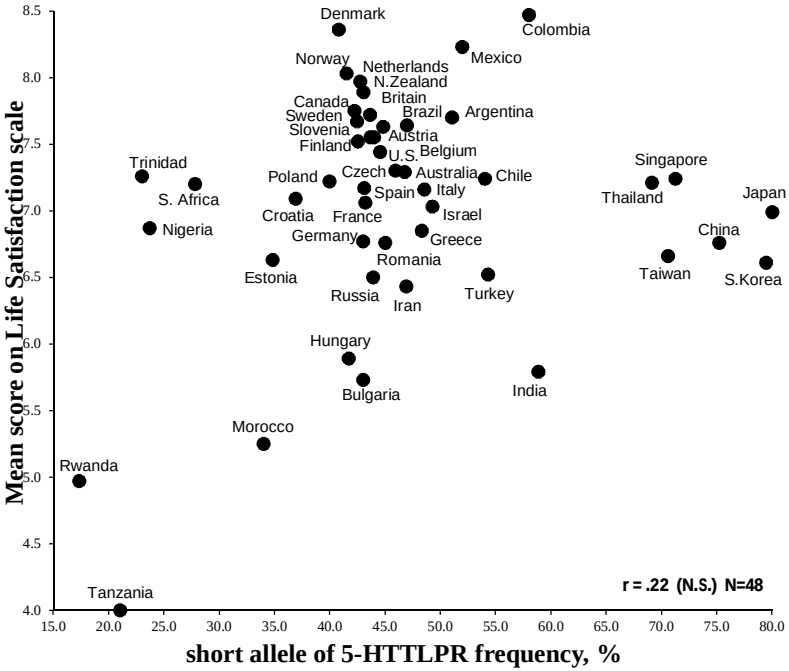

Figure 1 Life Satisfaction by 5-HTTLPR short allele frequency, %.
r = .22 (n.s.), N = 48.

Figure 1 shows the relationship between mean life satisfaction levels and the percentage of the population having the short allele of the serotonin transporter gene. The right-hand side of this figure shows a cluster of East Asian and Southeast Asian countries in which very high percentages of the population have the short allele – but these countries do not show the lowest happiness levels (they are about average). On the left-hand side of the figure, several African countries plus Trinidad (in which about half the population is of African origin) have the lowest percentages of the short allele; some of them show low levels of happiness but others show rather high levels. Though De Neve has presented convincing evidence that within a sample of U.S. students, those with the short allele tend to be significantly less satisfied with their lives than those with the long allele, countries in which a large share of the population has the short allele do *not* show

relatively low levels of happiness. Let us repeat, we do not view this as refuting De Neve's findings – but it does have significant implications about the interaction between societal-level and individual-level influences on happiness.

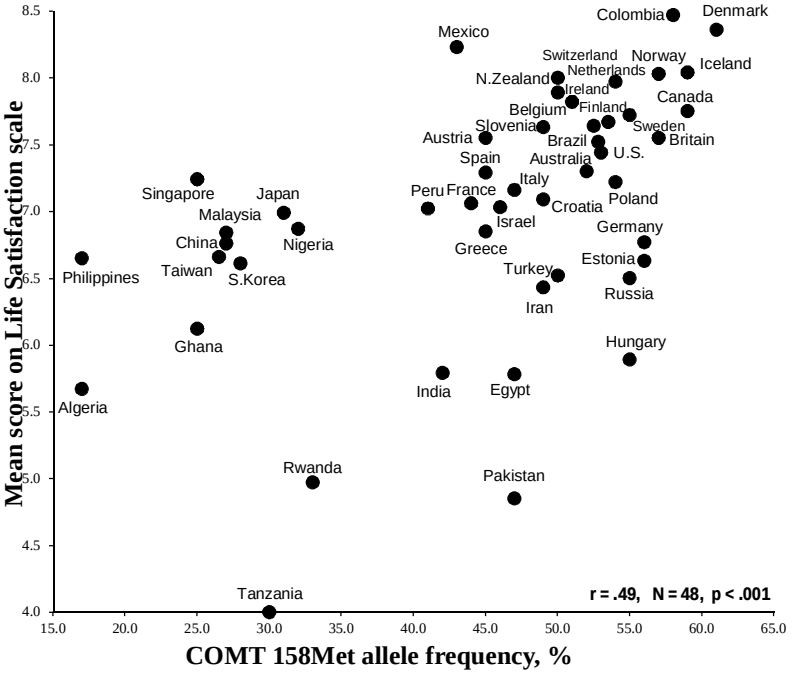

Figure 2 Life Satisfaction level by on COMT 158Met allele frequency
r = .49, p < .001 (N=48).

Figure 2 shows the relationship between happiness and the distribution of the 158Met allele in the COMT Val158Met polymorphism. It shows a clear tendency for the A allele to be linked with high levels of happiness, which is consistent with what physiological evidence would lead one to expect, since this allele is linked with higher dopamine levels in the brain. On the left side of this figure, we find a group of East Asian, Southeast Asian and African countries in which the populations tend to have low percentages of the A allele. This distribution of the gene does not seem to reflect the distance a given population has traveled in moving out of Africa, since it groups populations located far from Africa with populations still in Africa. The life satisfaction levels of this group range from very low to above the mean, but the overall tendency is for countries having a high percentage of the A allele to show the highest happiness levels. Here again, simple geo-

graphic determinism doesn't seem to work. Although many Northern European countries such as Denmark, Norway, Iceland and the Netherlands rank high on both variables, this is also true of such Latin American countries as Colombia, Mexico and Brazil. Since a substantial percentage of the population in the latter countries is of non-European descent, racial origin can not readily explain this pattern. We will propose an alternative explanation, which has a better fit with the empirical evidence.

Evidence from surveys carried out in scores of countries from 1981 to 2007 indicates that a sense of security is conducive to happiness and life satisfaction. Economic security is certainly important – one finds a .61 correlation between a country's per capita GDI and its mean life satisfaction score. But social tolerance is also important, so that rising levels of gender equality and tolerance of outgroups contributed to rising life satisfaction in most countries during 1981 to 2007.[29] Why is it that societies in which the 158Met allele of the COMT gene is widespread, are happier than others – while the populations of societies where the long allele of the 5-HTTLPR gene is widespread do not show relatively high happiness levels? This may reflect the fact that the COMT polymorphism has been found to be linked with pro-social behavior, while the 5-HTTLPR polymorphism has not.

Table 3 Correlations between gene allele distributions and indicators of tolerant, pro-social behavior

	5-HTTLPR short allele frequency, %	**COMT 158Met allele frequency, %**
Legislation concerning homosexuality scale: Same Sex Marriage is legal = 1 …death penalty for homosexuality = 8	**-.13** (48)	**-.60 ***** (48)
UN Gender Empowerment Measure (% of women in high-level positions in government, business and academic life)	**-.18** (44)	**.42 **** (43)
General tolerance factor: respondent supports gender equality in jobs, is relatively tolerant of homosexuality, accepts foreigners as neighbors (positive pole)	**-.03** (44)	**.54 ***** (43)
Materialist/Postmaterialist values index (Postmaterialist values are high)	**-.10** (48)	**.47 ***** (48)

* p < .05 ** p < .01 *** p <.001
Number of countries is in parentheses.

Table 3 provides societal-level evidence that supports previous findings from individual-level studies that the 158Met allele of the COMT gene is linked

with pro-social behavior. It shows the correlations between the two respective polymorphisms and two attitudinal measures, and two measures of the extent to which a society actually *is* tolerant. The first is an eight-point index of legislation concerning homosexuality, with scores ranging from "1" which indicates that (as of 2012) same-sex marriage was legal, moving through various stages of diminishing tolerance to a score of "8," indicating that homosexuality punishable by death. The A allele shows a -.60 correlation with this indicator, significant at the .001 level, while the short allele of 5-HTTLPR has no significant linkage. The second indicator is the UN Gender Empowerment Measure, which is based on the proportion of women holding positions of authority in government, business and academic life in a given country. Here again, the COMT Val158Met polymorphism shows a statistically significant relationship with an indicator of tolerant, pro-social behavior while the 5-HTTLPR polymorphism does not. Next, we examine a measure of tolerant attitudes based on representative national surveys carried out by the World Values Survey in scores of countries. The COMT Val158Met polymorphism shows a correlation that is significant in the expected direction at the .001 level while the 5-HTTLPR polymorphism has no significant linkage. Finally, we show the correlation with Materialist/ Postmaterialist values, a widely used measure of basic values that reflects the extent to which given respondents give top priority to economic and physical security, or to autonomy and self-expression. Postmaterialists tend to have grown up under relatively secure conditions and are significantly more tolerant of outgroups and more politically active than Materialists. Again, the COMTval158Met polymorphism shows a correlation that is statistically significant at the .001 level while the 5-HTTLPR polymorphism has no significant linkage.

We see no reason to doubt De Neve's finding that the long allele of the serotonin transporter is linked with relatively high levels of happiness at the individual level in the U.S. – but it seems to act only at the individual level. Moreover, De Neve's finding is based on data from the U.S. only. While the s-allele of the 5-HTTLPR is the risk allele for inferior mental health in most studies,[30] in some countries the l-allele has been reported to be the "risk allele."[31,32,33] These findings have led to the concept that *5-HTT* is a "plasticity gene"[34] that both alleles offer advantages but in different environments.[35] If these two different patterns existed in roughly equal numbers of countries, it would explain the neutral overall effect. The evidence examined here suggests that the A allele of COMTval15Met has cross-nationally consistent effects. Apparently, societies in which a large share of the population carries the A allele of COMTval158Met, have larger numbers of pro-social actors – and they consistently show significantly higher levels of social tolerance. As previous research indicates,[36] and as we will further

demonstrate below, social tolerance is conducive to happiness. It establishes a less stressful, more congenial environment. The populations of societies in which the 158Met allele of the COMT gene is widespread, not only have more tolerant attitudes – their societies themselves tend to be more tolerant, which is conducive to higher levels of life satisfaction. The long allele of 5-HTTLPR seems to raise the happiness levels of individuals within a given society but it does not seem conducive to the pro-social behavior that is linked with the COMT Val158Met polymorphism – and at the societal level, the positive effects of the serotonin transporter gene may be submerged by even stronger economic and social factors, such as democratic institutions or a high level of economic development, that are constants *within* any given society, and consequently cannot be analyzed in one-country studies.

3. The Impact of Societal-level Factors on Happiness

Massive societal-level factors can have a strong impact on virtually everyone within a given society, as recent Russian history illustrates. Most societies that experienced communist rule show relatively low levels of subjective well-being, even in comparison with societies at a lower economic level, such as India, Bangladesh, and Nigeria. Are these low levels of well-being a permanent baseline characteristic, possibly linked with genetic feature of their societies, or are they a relatively recent phenomenon linked with the collapse of communism? Time series data from Russia demonstrates that, under extreme conditions, life satisfaction levels can vary dramatically, as Figure 3 illustrates. Data from representative national samples of the Russian public are available from 1990 to 2011, and we can extend the time series even farther back to if we accept a 1982 survey in Tambov oblast as a proxy for Russia.*

The results indicate that, already in 1982, the subjective well-being of the Russian people was even lower than that of much poorer countries such as Nigeria, Bangladesh, Turkey, and India. Russia was experiencing rising alcoholism, absenteeism, and the collapse of the communist belief system – and the subjective well-being of its people was lower than that of countries with a fraction of their income. From this already-low level, Russian subjective well-being fell sharply, so that by 1990 the Russians manifested extreme malaise. Over half the population said they were dissatisfied with their lives as a whole. Within a year the communist system had collapsed, and the Soviet Union had broken up into successor states. Well-being continued to fall after the collapse, and in 1995 the overwhelming majority of the population said they were dissatisfied with their lives. Life satisfaction is normally very stable in advanced industrial societies. But it can and does

show sharp declines – and it seems significant that the dramatic decline of subjective well-being in Russia was followed by the collapse of the political, economic and social welfare systems, and the breakup of the Soviet Union. The sharp decline in subjective well-being experienced by the Russian people since 1982 is linked with traumatic historical events.

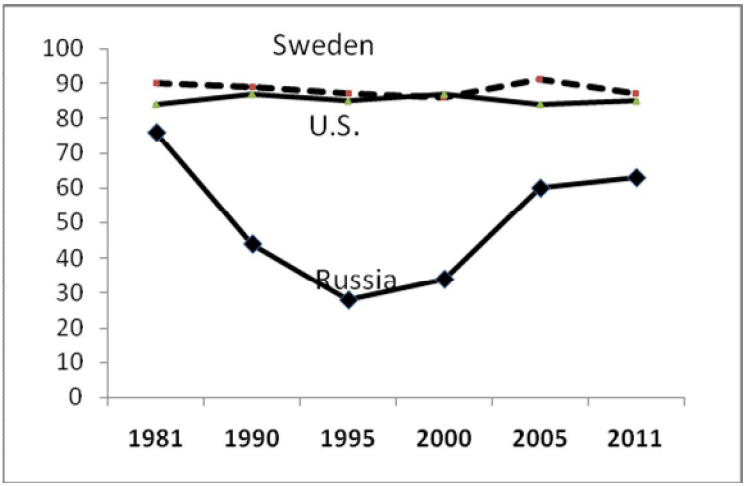

Figure 3 Life Satisfaction levels in Russia, United States and Sweden, 1981–2011 (percentage describing themselves as "satisfied" with their lives as a whole, i.e., choosing points 6–10 on 10-point scale on which 1 = completely dissatisfied and 10 = completely satisfied).

These findings in no way refute the claim that genetic factors play an important role in subjective well-being – there is compelling evidence that they do. But these findings indicate that we are not the slaves of our genes. Happiness levels vary a great deal and in part they vary with cultures and institutions that are constructed by human beings. Thus, the pursuit of happiness is not necessarily futile. Genetic factors seem to play an important role, but they do so in interaction with societal-level factors. To fully understand the implications of individual-level genetic findings, one must also take into account the impact of societal-level factors.

4. Multivariate Analysis

Life satisfaction levels vary greatly from one country to another. The percentage indicating they were "dissatisfied" with their lives as a whole (placing themselves on the lower half of a 10-point life satisfaction scale) ranges from 6 percent in The Netherlands, to 76 percent in Tanzania. Table 4

examines the impact of genetic variation on life satisfaction – together with the impact of economic development, social tolerance and other influences. As we have already seen, the 5-HTTLPR polymorphism has no significant impact on life satisfaction at the societal level. As Model 1 indicates, its linkage is weak and (if one expects the short allele to have a negative) even shows the wrong sign. But the 158Met allele of the COMT polymorphism shows a highly significant impact in the expected direction (Model 2). By itself, it explains 22 percent of the cross-national variation in life satisfaction. The two polymorphisms are negatively correlated, and when entered in the same regression equation this inflates the variance considerably, producing misleading results.

The distribution of both the short allele of 5-HTTPLR and the COMT-158Met allele predict that East Asian societies should be very low on life satisfaction, but in fact, the Far Eastern societies fall in the middle of the happiness range. Moreover, when both genes are included in the regression model, their effects are much stronger than in bivariate models. This curious effect is driven by the four East Asian societies in the sample (China, Japan, Singapore, and South Korea), which have extreme positions on the distribution of both genes and therefore have a strong leverage effect. But their leverage effects (very high on 5-HTTPLR and very low on COMT) sum close to zero in the multiple regression and the resulting fit is good, bringing their predicted life satisfaction to the middle of the range of life satisfaction.

Dropping the Far Eastern societies drastically changes the bivariate correlation between the short allele of 5-HTTPLR and the COMT 158Met allele: although the correlation is -.66 when they are included, the correlation becomes positive and mild when they are excluded. In the reduced subset of cases, the COMT gene retains its predictive value whereas the effect of the short allele on Life Satisfaction becomes even weaker.

It is possible that both genes have an impact on life satisfaction. African societies and East Asian societies are low on the COMT 158Met allele, but the Far Eastern societies, unlike the African ones, are also high on 5-HTTPLR. Caucasian societies are in the upper range on both genes. This roughly fits the empirical variation on life satisfaction. However, most of the cases for which we have data on both genes, come from societies with large proportions of Caucasian populations. Therefore we do not have enough variation to be certain of the effect of 5-HTTPLR, although we do have enough variation on COMT to proceed with the analysis. For this reason and because it has very little explanatory power, we exclude the 5-HTTLPR polymorphism from subsequent analyses.

Table 4 Predictors of Life Satisfaction: national-level regression analysis (dependent variable is nation's mean on 10-point life satisfaction scale, 1=completely dissatisfied… 10=completely satisfied)

Independent Variables:	**Mod.1**	**Mod. 2**	**Mod. 3**	**Mod. 4**	**Mod. 5**	**Mod. 6**	**Mod. 7**	**Mod. 8**	**Mod.9**	**Mod.10**
5-HTTLPR short allele frequency, %	**.22**	__	__	__	__	__	__	__	__	__
COMT 158Met allele frequency, %	__	**.49*** **	**.25***	**.24***	**.17**	**.03**	**.09**	**.23**	__	__
GDP/capita in 2000	__	__	**.53*** **	__	**.33***	**.12**	__	__	__	__
Materialist/ Postmaterialist values	__	__	__	**.54*** **	**.36** **	**.26***	**.26***	**.25***	**.28***	**.28***
Tolerance: Legislation concerning Homosexuals	__	__	__	__	__	**-.48** **	**-.37***	**-.37***	**-.46** **	**-.43** **
Composite Political Risk Score	__	__	__	__	__	__	**.27***	**.28***	**.24***	**.25***
Caucasian race as % of country's population	__	__	__	__	__	__	__	**-.18**	**-.07**	__
Historical parasite vulnerability (Fincher)	__	__	__	__	__	__	__	__	__	__
Constant	6.58	5.26	5.38	1.32	2.71	5.15	2.85	2.66	3.45	3.29
Adjusted R-squared	**.01**	**.22**	**.43**	**.44**	**.50**	**.58**	**.62**	**.63**	**.62**	**.63**
N =	47	47	47	47	47	47	47	47	47	47

Cell entry is standardized regression coefficient. Signif. levels:***p< .001; ** p < .01; * p<.05

Source: genetic data compiled from articles in scientific journals; attitudinal variables from latest available survey from 1981-2011 World Values Surveys and European Value Study; economic data from World Bank, *World Development Indicators*; Legislation concerning homosexuals from LGBT Portal; Composite Political Risk scores from *International Country Risk Guide*.

As previous analyses have found, the transition from subsistence-level poverty to a fair degree of economic security brings a considerable increase in life satisfaction. When we add a society's per capita GDP to the regression, it and the COMT158Met polymorphism explain fully 43 percent of the cross-national variation in life satisfaction (Model 3). The prevalence of Postmaterialist values has fully as much explanatory power: together with the COMT158Met polymorphism, it explains 44 percent of the cross-national variance (Model 4). These three variables combined explain fully half of the variance (Model 5) and when we add the indicator of tolerance of homosexuals, Model 6 explains 58 percent of the cross-national variation in life satisfaction. As expected, the two indicators of tolerant, pro-social conditions have strong impacts on a society's happiness level; they overlap with the genetic factor and with GDP per capita to such an extent that the contributions of the latter two variables drop below significance in Model 6. Model 7 drops GDP per capita and adds a Composite Political Risk indicator that reflects to the degree to which given societies have stable, non-corrupt governments with low levels of internal and foreign conflict, bringing the explained cross-national happiness variance up to 63 per cent. In this model, the indicators of tolerance, Postmaterialist values and stable polities explain almost all of the variance – but these characteristics are most likely to be present in prosperous societies where the COMT 158Met allele is relatively widespread.

5. Geographic Clustering

Let's consider the impact of geographic clustering. If it is present, the correlations we find between COMT alleles and happiness (for example) might simply reflect population segmentation, in which given populations became geographically separated and then by genetic drift, came to differ on many genes – so that any correlation between a specific gene and a given attribute might not reflect a causal linkage but simply the fact that they happen to go together in different populations.

Commenting on Chiao and Blizinsky's[37] analysis of the cultural impact of cross-national variation in the serotonin transporter gene 5-HTTLPR, Eisenberg and Hayes[38] point out that their units of analysis may not be independent: the linkage between individualist-collectivist cultures and the 5-HTTLPR gene mainly reflects the contrast between a cluster of five East Asian societies that are high on both the short allele of this gene and on collectivist cultures; and a cluster of 22 countries that are low on both attributes – and are populated mainly by people of European/Caucasian descent. Within these two clusters, they find no significant linkage between the short allele of 5-HTTLPR and collectivist cultures. Similarly, De Neve

et al. (2012) note that the association between Life satisfaction and the 5-HTTLPR gene that they find, might be due to population stratification rather than reflecting a causal link between genes and happiness. To deal with this possibility, they control for the respondent's race in their analysis, finding that the linkage does not disappear.

A larger and more diverse set of 48 countries is examined here than the 29 countries analyzed by Chiao and Blizinski; and, as Figure 2 indicates, the relationship between happiness and the COMT 158Met allele does not break down into an East Asian vs. European cluster. Nevertheless it is evident that the populations of East Asian, Southeast Asian and African countries do have a significantly lower incidence of the Met allele than the populations of European, South Asian and Latin American countries. To partly control for the impact of population stratification, Models 8 and 9 introduce a variable that measures the percentage of each country's population that is of Caucasian descent (including those living outside Europe). By itself, this variable explains less than one percent of the cross-national variance in life satisfaction, and when added to the regression equation in Model 8, it raises the explained variance by only one point, from 62 percent to 63 percent, and is not statistically significant. Models 9 and 10 reduce the number of variables included by dropping first the COMT 158Met allele, and then the percentage of the population that is of Caucasian descent. Doing so does not reduce the amount of explained variance: our most parsimonious model, Model 10, still explains 63 percent of the cross-national variance with only three independent variables. The explanatory models presented here do not seem to reflect a European/non-European dichotomy.

As Model 10 indicates, we can explain a large proportion of the cross-national variation in happiness with three variables (1) Postmaterialist values, which reflect the extent to which the population was raised under relatively high levels of economic and physical security; (2) social tolerance – itself, an indicator of relatively secure social conditions; and (3) relatively secure political conditions. But the evidence also indicates that these factors are linked with prosperity and genetic factors, which by themselves explain 43 percent of the cross-national variance.

Though the COMT factor eventually drops out of the model, this is consistent with the interpretation that a high frequency of the relevant COMT 159Met allele helps make pro-social and tolerant attitudes and institutions more likely to emerge. Though the latter attributes are closely linked with the COMT Val158Met polymorphism, they have emerged only recently and cannot have caused the genetic phenomenon. But what did cause it?

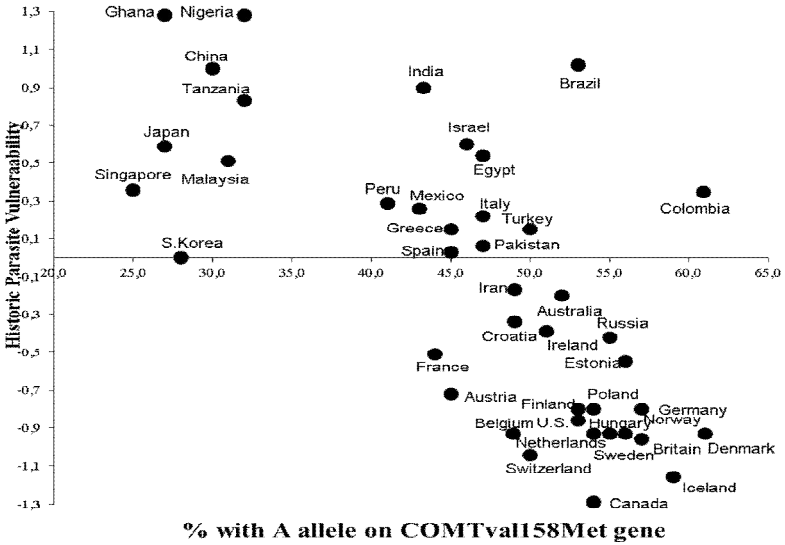

Figure 4 Frequency of COMT 158Met allele and historical parasite prevalence. r = -.71 p < .000 (N=45). Historic parasite prevalence from Fincher et al., 2008.

Neither a country's distance from Africa nor its racial composition seem to explain the prevalence of the COMT 158Met allele. But historic parasite prevalence may play an important role.[39] It has been argued convincingly that, in societies where the threat of infectious disease is strong, avoidance of strangers is conducive to survival, conferring an evolutionary advantage on any genes that happen to be linked with avoidance of strangers. This relatively inward-looking and xenophobic outlook would be conducive to survival in these circumstances, but it would come at a cost: it would be less conducive to the pro-social behavior that seems to be linked with higher levels of life satisfaction. Conversely, societies with lower levels of parasite prevalence would have higher levels of pro-social behavior, which is linked with cooperative activities and higher levels of happiness. Thus, it seems possible that genetic factors were involved in the selection of such behavior. As Figure 4 indicates, the populations of societies that historically had high prevalence of infectious disease tend to show lower levels of the 158Met allele than societies that had low parasite prevalence. The overall correlation is -.71, which suggests that as much as half of the cross-national variation in the prevalence of the 158Met allele might reflect the historic parasite load or related factors.

6. The Impact of Economic Development on Happiness

Though family income explains only about 3 percent of the variance in life satisfaction at the individual level, we find a .61 correlation between per capita GDP and mean life satisfaction scores at the national level, as Table 2 indicates. This suggests that economic development might explain as much as 37 percent of the cross-national variance. In other words, there is a huge difference between the apparent impact of economic factors on life satisfaction at the individual level and at the societal level. In part, this reflects the fact that there is a much wider range of variation between nations than within nations. For example, within the U.S., the richest state (Connecticut) has a per capita income twice as high as that of the poorest state (Mississippi). But on the cross-national scale, World Bank data indicates that the world's richest nation (Norway) has a per capita income (adjusted for purchasing power parity) that is 300 times as high as that of the poorest nation (Democratic Republic of the Congo). Moreover, the data cited by De Neve et al. concerning the modest impact of income on subjective well-being are from high-income countries. But the impact of income on life satisfaction follows a curve of diminishing returns: among the publics of low-income countries it has a considerably stronger impact than it does among the publics of high-income countries. This does not refute the finding that income has a relatively modest impact on happiness *within* the U.S. today – it does. But this finding has somewhat misleading implications for policy makers: the fact that economic development has a .61 national-level correlation with life satisfaction suggests that economic development can have a considerable impact on human happiness. If massive social changes raise or lower the happiness levels of almost everyone in a society, one would continue to observe relatively weak correlations between income and happiness within that society – although the society as a whole experienced traumatic changes in happiness levels. This is precisely what seems to have occurred in Russia during the past four decades.

Things do not necessarily work in the same way at the individual level and the societal level. The long allele of the 5-HTTLPR polymorphism seems significantly linked with happiness at the individual level, but the populations of countries in which this allele is widespread do not seem to be happier than the populations of countries in which it is rare. On the other hand, evidence from 48 countries indicates that populations in which the 158Met allele of the COMTval158Met polymorphism is relatively widespread are significantly happier than the populations of countries in which it is relatively rare. This suggests, but does not prove, that the COMTval-158Met polymorphism may complement the 5-HTTLPR polymorphism in helping to shape the life satisfaction levels of individuals; individual-level

analysis will be needed to demonstrate whether this is true. In any case, there is evidence that the COMT 158Met encourages pro-social behavior that is conducive to higher life satisfaction levels in given societies.

Let us perform a still more demanding test of geographic genetic clustering. Building on earlier exercises in genetic mapping,[40] we gathered data on 79 STR allele frequencies of five genetic markers used in forensic genetic testing to identify people's origins. We obtained data from the 39 countries shown in Figure 5 (countries such as the U.S., Australia or Argentina, whose population are mainly immigrants from other countries on this map, are not included). Figure 5 shows the genetic relationships between the populations of these countries, based on a principal components factor analysis of each country's mean score on the 79 STR alleles. The horizontal dimension shows each country's loading on the first principal component, which explains 42% of the cross-national variance. The vertical dimension reflects the second principal component, which explains 20% of the cross-national variance. We used the forensic STR system because these data are available for many populations, including some not studied for other genes.[41]

The MDS plot in Figure 5 shows five clear geographic clusters, grouping countries in sub-Saharan Africa, South America, South Asia and North Africa, East and Southeast Asia, and Europe. The distances on this Figure can be interpreted as roughly reflecting the geographic distance traveled in humanity's emigration out of Africa – though South America (geographically the most remote region) is relatively close to the African cluster and East Asia is closer than Europe.

But the horizontal dimension, based on the first principal component, could be interpreted as reflecting the degree of parasite prevalence, to which it is correlated at r = -.86. This dimension is also correlated rather strongly with a society's per capita GDP (r = .55). And it is even more strongly correlated with the distribution of the COMT polymorphism, at r = .76. Consequently, when both variables are entered in a multiple regression on Life Satisfaction, both effects become insignificant.

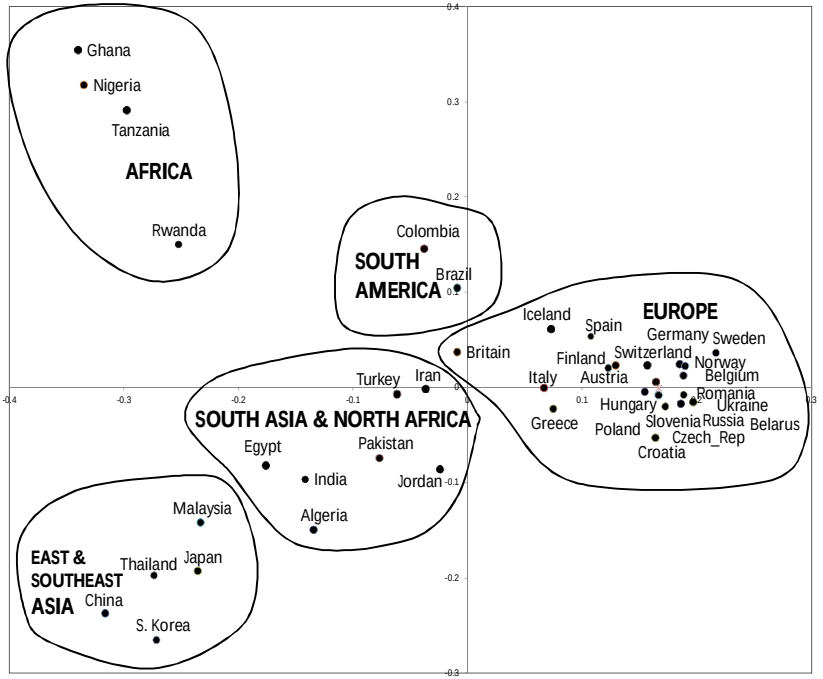

Figure 5 Multidimensional Scaling Plot Depicting Genetic Relationships between Populations of 39 Countries.

The horizontal dimension shows each country's loading on the first principal component from a factor analysis of 39 countries' mean scores on each of 79 STR alleles; the vertical dimension reflects the second principal component.

7. Conclusion

Though De Neve has presented convincing evidence that, within a sample of U.S. students, those with the short allele tend to be significantly less satisfied with their lives than those with the long allele, countries in which a large share of the population has the short allele do *not* show relatively low levels of happiness. On the other hand, the COMT 158Met allele does show a statistically significant linkage with life satisfaction, and in the expected direction. We do not view this as refuting De Neve's findings about individual-level linkages within the U.S., but it does have significant implications concerning the interaction between societal-level and individual-level influences on happiness.

If two variables go together at the individual level, they usually – but not necessarily – also go together at the level of large groups. In fact, national-level linkages can be stronger or weaker than individual-level linkages or even have opposite polarity. National-level findings do not refute individual-level findings, but they can help us understand how individual-level genetic factors interact with societal factors in shaping a society's level of happiness. As we have shown, societal-level phenomena seem to play at least as important a role as genetic differences in shaping a given country's mean happiness level.

The analysis in Figure 5 supports other findings indicating that genetic variation tends to be geographically clustered. This implies that any correlation between gene X and a given attribute might not reflect a causal linkage, but simply the fact that they happen to go together in different populations. The real cause might be another gene that is closely linked with gene X – or even some cultural or political or economic factor that is closely correlated with gene X.

This is certainly possible. We find strong correlations between the COMT allele and a whole cluster of genetic polymorphisms *and* certain cultural zones *and* high levels of economic development *and* high levels of social tolerance. At this point, we can not be certain which of many related genes is driving the process if any. It is conceivable that certain types of pre-modern societies might have been able to affect genetic pools by encouraging pro-social behavior and suppressing its opposite. But it seems unlikely that high levels of economic development or a specific culture is the root cause of the genetic variation – which almost certainly preceded the emergence of these relatively recent phenomena. And it is even more implausible that the strong correlations that we find between the COMT alleles and current societal features such as the UN Gender Empowerment Measure, and legislation concerning homosexuality simply reflect population segmentation and genetic drift. These are very recent developments in which the publics of 48 different countries independently began to accept gender equality and to tolerate homosexuality in varying degrees. The strong correlations that we find between this wide range of genetic, economic and social phenomena seem too strong to result from random drift: there is almost certainly an underlying causal process, though we have only begun to sort it out.

The fact that we find a correlation of -.60 between the 158Met allele and the degree to which homosexuality is repressed in given countries, suggests that there may be a causal link between the distribution of this allele and social tolerance. This supposition is supported by the fact that we also find highly significant correlations between this allele and other indicators of social tolerance. We know that economic security is conducive to tolerance, but these societies are not more tolerant simply because they

are relatively prosperous: the linkages persist when we control for per capita GDP. These linkages do not prove that the COMT polymorphism causes tolerance, but they provide a prima facie indication that this genetic factor may be involved – perhaps in connection with other genes that have not yet been identified. Logically, the next step is to seek individual-level evidence that the COMT polymorphism is linked with happiness.

We suggest that a major cause of the systematic clustering of genetic characteristics may be climatic conditions linked with relatively high or low levels of parasite prevalence, in accordance with results of Fumagalli et al., 2011.[42] This may lead certain populations to develop gene pools linked with different levels of avoidance of strangers, which helped shape different cultures, both of which eventually helped shape economic development. Still more recently, this combination of distinctive cultural, economic and genetic factors has led some societies to more readily adopt gender equality and high levels of social tolerance, than others. Though economic development tends to make all societies more tolerant and open to gender equality, these findings suggest that cross-national differences in how readily these changes are accepted may reflect genetically-linked cultural predispositions.

NOTE

*It was not possible to carry out the first wave of the Values Surveys in Russia, but our Soviet colleagues were able carry it out in Tambov oblast, a region they considered representative of Russia as a whole. In order to verify this assumption, we surveyed Tambov oblast again in 1995, along with a separate survey of the Russian republic. The results from Tambov and Russia in 1995 were similar: for example, on life satisfaction, Russia ranked 61st and Tambov 62nd among the 65 societies surveyed. Our Russian colleagues' belief that Tambov was reasonably representative of Russia as a whole seems justified.

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Internet Appendix

Table A1 *5-HTTLPR* genotype and allele frequencies in studied countries

Study	Country	Pop	N	M/F	SS	%	SL	%	LL	%	2N	S	%	L	%	
Sookoian S et al. Obesity (Silver Spring). 2008; 16(2):488-91.	Argentina	GP	1329	1329/0	356	26.79%	651	48.98%	322	24.23%	2658	1363	51.28%	1295	48.72%	a
Sookoian S et al. Sleep. 2007; 30(8):1049-53.	Argentina	GP	683	683/0	184	26.94%	326	47.73%	173	25.33%	1366	694	50.81%	672	49.19%	a
TOTAL			2012	2012/0	540	26.84%	977	48.56%	495	24.60%	4024	2057	51.12%	1967	48.88%	
AVG						26.86%		48.36%		24.78%			51.04%		48.96%	
Jorm AF et al. Mol Psychiatry 1998; 3: 449-451.	Australia	GP	759	357/402	155	20.42%	350	46.11%	254	33.47%	1518	660	43.48%	858	56.52%	a, b
Naylor L et al. Mol Med. 1998; 4(10):671-4.	Australia	SCZ/GP	120	-	31	25.83%	59	49.17%	30	25.00%	240	121	50.42%	119	49.58%	a
Olsson CA et al. Mol Psychiatry. 2005; 10(9):868-76.	Australia	GP* (VAHCS)	752	309/443	150	19.95%	363	48.27%	239	31.78%	1504	663	44.08%	841	55.92%	a
Wilhelm K et al. Br J Psychiatry. 2006;188:210-5.	Australia	GP	127	42/85	27	21.26%	62	48.82%	38	29.92%	254	116	45.67%	138	54.33%	a
TOTAL			1758	-	363	20.65%	834	47.44%	561	31.91%	3516	1560	44.37%	1956	55.63%	
AVG						21.87%		48.09%		30.04%			45.91%		54.09%	
Thierry N et al. Eur Neuropsychopharmacol 2004; 14(1): 53-58.	Austria	SAD/GP	132	0/132	27	20.45%	64	48.48%	41	31.06%	264	118	44.70%	146	55.30%	a
Willeit M et al. Mol Psychiatry. 2003; 8(11):942-6.	Austria	SAD/GP	284	45/239	53	18.66%	136	47.89%	95	33.45%	568	242	42.61%	326	57.39%	a
TOTAL			416		80	19.23%	200	48.08%	136	32.69%	832	360	43.27%	472	56.73%	
AVG						19.56%		48.19%		32.26%			43.65%		56.35%	

Wichers et al. Am J Med Genett Part B. 2008, 147B: 120-123																
	Belgium	GP	394	0/394	82	20.81%	184	46.70%	128	32.49%	788	348	44.16%	440	55.84%	d
TOTAL			394	0/394	82	20.81%	184	46.70%	128	32.49%	788	348	44.16%	440	55.84%	
AVG			394		82	20.81%	184	46.70%	128	32.49%			44.16%		55.84%	
		GP														
Costa JE et al. J Oral Sci. 2008; 50(2):193-8.	Brazil	(Periodontis)	132	82/50	52	39.39%	54	40.91%	26	19.70%	264	158	59.85%	106	40.15%	
																a
Grevet EH et al. J Neural Transm. 2007; 114(12): 1631-6.		ADHD/G														
	Brazil		548	-	102	18.61%	303	55.29%	143	26.09%	1096	507	46.26%	589	53.74%	
		P														a
Marques FZ et al. Psychiatr Genet. 2006; 16(3):125-31																
	Brazil	Alc/GP	332	332/0	67	20.18%	174	52.41%	91	27.41%	664	308	46.39%	356	53.61%	
																a
Meira-Lima I et al. Genes Brain Behav. 2004; 3(2):75-9.																
	Brazil	OCD/GP	279	-	60	21.51%	138	49.46%	81	29.03%	558	258	46.24%	300	53.76%	
																a
Oliveira JR et al. Mol Psychiatry. 2000; 5(4):348-9.																
	Brazil	DT/BPD/	389	-	67	17.22%	175	44.99%	147	37.79%	778	309	39.72%	469	60.28%	
		MDD/GP														
																a
Wachleski C et al. Neurosci Lett. 2008; 431(2):173-8.																
	Brazil	PanD	67	14/53	14	20.90%	30	44.78%	23	34.33%	134	58	43.28%	76	56.72%	
																a
TOTAL			1747		362	20.72%	874	50.03%	511	29.25%	3494	1598	45.74%	1896	54.26%	
AVG						22.97%		47.97%		29.06%			46.96%		53.04%	
Mendlewicz J et al. Eur J Hum Genet. 2004 May 12 (5): 377-82, and Radka Kaneva, personal communication																
	Bulgaria	GP	457		77	16.85%	233	50.99%	147	32.17%	914	387	42.34%	527	57.66%	
TOTAL			457		77	16.85%	233	50.99%	147	32.17%	914	387	42.34%	527	57.66%	
AVG			457		77	16.85%	233	50.99%	147	32.17%	914	387	42.34%	527	57.66%	

Mileva-Seitz et al. Genes, Brains, and Behavior 2011, 10:325-333	Canada	GP	266	0/266	50	18.70%	147	55.40%	69	25.90%	532	247	46.43%	285	53.57%	
Ni et al. Journal of Psychiatric Research 2006, 40:448-453	Canada	GP	269		49	18.22%	129	47.96%	91	33.83%	538	227	42.19%	311	57.81%	
TOTAL			535		99	18.37%	276	51.59%	160	29.91%	1070	474	44.30%	596	55.70%	
AVG						18,46%		51,68%		29,87%			44,31%		55,69%	
Sanhueza et al. Rev Med Chile 2011, 139:1261-1268.	Chile	GP	91		29	31.90%	40	43.90%	22	24.20%	91	49	54.00%	42	46.00%	
TOTAL			91		29	31.90%	40	43.90%	22	24.20%	91	49	54.00%	42	46.00%	
AVG						31.90%		43.90%		24.20%			54.00%		46.00%	
Forero et al. Journal of Neuro Transmission 2006, 113:1253-1262	Colombia	GP	84		45	53.60%	25	29.80%	14	16.70%	168	115	68.50%	53	31.50%	
Ospina-Duque et al. Neuroscience Letters 2000, 292: 199-202	Colombia	GP	112		29	26.00%	61	54.00%	22	20.00%	224	119	53.00%	105	47.00%	
Perea et al. Journal of Affective Disorders 2012, 136: 767-774	Colombia	GP	302		89	29.50%	152	50.30%	61	20.20%	604	332	55.00%	272	45.00%	
TOTAL			498		163	32.73%	238	47.79%	97	19.48%	996	566	56.83%	430	43.17%	
AVG						36.37%		44.70%		18.97%			58.83%		41.17%	
Pivac et al. Neuroscience Letters 2009, 4: 45-48	Croatia	GP	520		67	12.88%	238	45.78%	215	41.35%	520	186	35.77%	334	64.23%	
Noskova et al. Prog Neuropsychopharmacol Biol Psychiatry.2008, 32: 1735-1739	Croatia	GP	665		95	14.30%	316	47.50%	254	38.20%	1330	505	38.00%	825	62.00%	
Hranilovic et al. Biol. Psychiatry 2003, 54: 884-889	Croatia	MDD	432		59	13.66%	212	49.07%	161	37.27%	864	330	38.19%	534	61.81%	
TOTAL			1617		221	13.67%	766	47.37%	630	38.96%	2714	1021	37.62%	1693	62.38%	
AVG						13.61%		47.45%		38.94%			37.32%		62.68%	

Martaskova et al. Folia Biologica 2009, 55:192-197																
	Czech Republic	GP	65	0/65	13	20.00%	30	46.10%	22	33.90%	130	56	43.10%	74	56.90%	
TOTAL			65		13	20.00%	30	46.10%	22	33.90%	130	56	43.10%	74	56.90%	
AVG						20.00%		46.10%		33.9*%			43.10%		56.90%	
Togsverd M et al.		GP*														
J Affect Disord. 2008;	Denmark	(PERF)	1369	0/1369	238	17.38%	641	46.82%	490	35.79%	2738	1117	40.80%	1621	59.20%	
106(1-2):169-72.																a
TOTAL			1369	0/1369	238	17.38%	641	46.82%	490	35.79%	2738	1117	40.80%	1621	59.20%	
AVG						17.38%		46.82%		35.79%			40.80%		59.20%	
Maron E et al. Int J																
Neuropsychopharmacol.	Estonia	PanD/GP	373	-	45	12.06%	173	46.38%	155	41.55%	746	263	35.25%	483	64.75%	
2005; 8(2):261-6.																a
		GP*														
Paaver M et al. Prog	Estonia	(EYHS/	435	-	55	12.64%	189	43.45%	191	43.91%	870	299	34.37%	571	65.63%	
Neuropsychopharmacol Biol		ECPBHS)														
Psychiatry. 2008; 32(5):1263-8.																b
TOTAL			808		100	12.38%	362	44.80%	346	42.82%	1616	562	34.78%	1054	65.22%	
AVG						12.35%		44.91%		42.73%			34.81%		65.19%	
		Alc														
Mazzanti CM et al. Arch	Finland	CO/GP	397	337/60	76	19.14%	196	49.37%	125	31.49%	794	348	43.83%	446	56.17%	
Gen Psychiatry 1998; 55:																a
936-940.																
		GP*		1704/												
Munafò MR et al. Am J																
Med Genet B Neuropsychiatr	Finland	(NFBC)	3872	2168	661	17.07%	1859	48.01%	1352	34.92%	7744	3181	41.08%	4563	58.92%	
Genet. 2009; 150B(2):271-81.																
																b
TOTAL			4269		737	17.26%	2055	48.14%	1477	34.60%	8538	3529	41.33%	5009	58.67%	
AVG						18.11%		48.69%		33.21%			42.46%		57.55%	

Anderson GM et al. Mol Psychiatry. 2002;7(8):831-6.	France	Aut	31	19/12	4	12.90%	16	51.61%	11	35.48%	62	24	38.71%	38	61.29%	
																a
Bellivier F et al. Am J Med Genet. 2001;105(8):758-60.	France	GP/NFT1	272	-	42	15.44%	138	50.74%	92	33.82%	544	222	40.81%	322	59.19%	
																a
Bellivier F et al. Neurosci Lett. 1998; 255(3): 143-6.		UPD/BP														
	France	D/ GP	348	-	66	18.97%	180	51.72%	102	29.31%	696	312	44.83%	384	55.17%	
																a
Chabane N et al. Neurosci Lett. 2004; 363(2): 154-6.	France	OCD/GP	277	169/108	46	16.61%	138	49.82%	93	33.57%	554	230	41.52%	324	58.48%	
																a
Courtet P et al. Biol Psychiatry. 2004;55(1):46-51.	France	SA	76	12/64	22	28.95%	39	51.32%	15	19.74%	152	83	54.61%	69	45.39%	
																a
Hammoumi S et al. Alcohol. 1999; 17(2)**:** 107-12.	France	Alc/GP	140	-	29	20.71%	57	40.71%	54	38.57%	280	115	41.07%	165	58.93%	
																a
Limosin F et al. J Psychiatr Res. 2005; 39(2): 179-82	France	Alc	100	48/52	12	12.00%	52	52.00%	36	36.00%	200	76	38.00%	124	62.00%	
																a
Power T et al. Neurobiol Aging. 2010;31(5):886-7.	France	GP	1421	-	309	21.75%	687	48.35%	425	29.91%	2842	1305	45.92%	1537	54.08%	
																a
TOTAL			2665		530	19.89%	1307	49.04%	828	31.07%	5330	2367	44.41%	2963	55.59%	
AVG						18.42%		49.53%		32.05%			43.18%		56.82%	

Hoefgen B et al. Biol Psychiatry. 2005; 57(3):247-51.	Germany	MDD/GP	1289	-	226	17.53%	628	48.72%	435	33.75%	2578	1080	41.89%	1498	58.11%	a
Jacob CP et al. Am J Psychiatry 2004; 161(3): 569-572.	Germany	PerD/GP	601	71/210	95	15.81%	302	50.25%	204	33.94%	1202	492	40.93%	710	59.07%	a
Koller G et al. Psychiatr Genet. 2008; 18(2):59-63	Germany	Alc	368	287/81	64	17.39%	195	52.99%	109	29.62%	736	323	43.89%	413	56.11%	a
Lang UE et al. Neuropsychobiology 2004; 49: 182-184.	Germany	GP	228	115/113	41	17.98%	102	44.74%	85	37.28%	456	184	40.35%	272	59.65%	a
Preuss UW et al. Biol Psychiatry. 2001; 50(8):636-9.	Germany	Alc/GP	280	187/93	43	15.36%	145	51.79%	92	32.86%	560	231	41.25%	329	58.75%	a
Preuss UW et al. Psychiatry Res. 2000; 96(1):51-61.	Germany	Alc	72	58/14	10	13.89%	42	58.33%	20	27.78%	144	62	43.06%	82	56.94%	a
Retz W et al. Neurosci Lett 2002; 319: 133-136.	Germany	GP	169	169/0	28	16.57%	94	55.62%	47	27.81%	338	150	44.38%	188	55.62%	a
Rujescu D et al. Psychiatr Genet. 2001; 11(3): 169-72	Germany	SA/GP	309	122/187	46	14.89%	148	47.90%	115	37.22%	618	240	38.83%	378	61.17%	a
Schmitz A et al. Pers Indiv Differ 2007; 42: 789-799.	Germany	GP	410	148/262	71	17.32%	196	47.80%	143	34.88%	820	338	41.22%	482	58.78%	a
Stamm TJ et al. Psychiatr Genet. 2008;18(2):92-7.	Germany	DIPt	50	21/29	9	18.00%	19	38.00%	22	44.00%	100	37	37.00%	63	63.00%	a
Strobel A et al. Z Different Diagnost Psychol 2000; 21: 194-199.	Germany	Paper copy not available	134	47/87	26	19.40%	69	51.49%	39	29.10%	268	121	45.15%	147	54.85%	d
Vormfelde SV et al. J Psychiatr Res 2006; 40(6): 568-576.	Germany	GP	195	97/98	69	35.38%	90	46.15%	36	18.46%	390	228	58.46%	162	41.54%	a

Stefanis et al. Genes, Brains, and Behavior 2011, 10: 536-541	Greece	GP	1594	1594/0	355	22.30%	764	47.90%	475	29.80%	3188	1474	46.24%	1714	53.76%	
TOTAL			1594	1594/0	355	22.30%	764	47.90%	475	29.80%	3188	1474	46.24%	1714	53.76%	
AVG			1594	1594/0	355	22.30%	764	47.90%	475	29.80%	3188	1474	46.24%	1714	53.76%	
Gonda X et al. J Affect Disord. 2009; 112 (1-3):19-29.	Hungary	GP	138	0/138	19	13.77%	69	50.00%	50	36.23%	276	107	38.77%	169	61.23%	a
Juhasz G et al. J Neurogenet. 2003; 17(2-3):231-40.	Hungary	GP (migraine)	227	0/227	46	20.26%	111	48.90%	70	30.84%	454	203	44.71%	251	55.29%	a
Szekely A et al. Am J Med Genet Part B 2004; 126B(1): 106-110.	Hungary	GP	151	68/89	29	19.21%	69	45.70%	53	35.10%	302	127	42.05%	175	57.95%	c
Szilagyi A et al. Headache. 2006 Mar;46(3):478-85.	Hungary	(migraine)	551	294/257	105	19.06%	245	44.46%	201	36.48%	1102	455	41.29%	647	58.71%	c
TOTAL			1067	362/827	199	18.65%	494	46.30%	374	35.05%	2134	892	41.80%	1242	58.20%	
AVG						18.07%		47.26%		34.66%			41.71%		58.29%	
Banerjee E et al. Am J Med Genet B Neuropsychiatr Genet. 2006; 141B(4):361-6.	India	ADHD/ Parents/ GP	332	-	119	35.84%	141	42.47%	72	21.69%	664	379	57.08%	285	42.92%	a
Guhathakurta S et al. Brain Res. 2006; 1092(1):28-35.	India	Aut/ Parents/ GP	355	-	147	41.41%	167	47.04%	41	11.55%	710	461	64.93%	249	35.07%	ab
Kumar HB et al. Psychiatr Genet. 2007;17(5):253-60. Erratum in: Psychiatr Genet. 2007;17(6):360.	India	PP/BPD/ GP	320	0/320	100	31.25%	149	46.56%	71	22.19%	640	349	54.53%	291	45.47%	a

TOTAL			1007		366	36.35%	457	45.38%	184	18.27%	2014	1189	59.04%	825	40.96%	
AVG						36.17%		45.36%		18.47%			58.85%		41.15%	
Safarinejad.																
Journal of Urology	Iran	GP	82	82/0	17	20.70%	30	36.90%	35	42.70%	113	53	46.90%	60	53.10%	
2009, 181: 2656-2661																
TOTAL			82		17	20.70%	30	36.90%	35	42.70%	113	53	46.90%	60	53.10%	
AVG						20.70%		36.90%		42.70%			46.90%		53.10%	
Arbelle S et al.																
Am J Psychiatry. 2003;	Israel	GP	98	-	18	18.37%	48	48.98%	32	32.65%	196	84	42.86%	112	57.14%	
160(4): 671-6.																a
Auerbach J et al.																
Mol Psychiatry. 1999;	Israel	GP	77	-	26	33.77%	29	37.66%	22	28.57%	154	81	52.60%	73	47.40%	
4(4):369-73.																a
Ebstein RP et al.																
Mol Psychiatry 1997;	Israel	GP	121	67/54	32	26.45%	66	54.55%	23	19.01%	242	130	53.72%	112	46.28%	
2: 224-226.																a
Kotler M et al.																
Mol Psychiatry. 1999;	Israel	Her/ GP	403	-	98	24.32%	198	49.13%	107	26.55%	806	394	48.88%	412	51.12%	
4(4): 313-4.																a
		ADHD/H														
Manor I et al.		RR														
Am J Med Genet. 2001;	Israel	Control/	1194	-	236	19.77%	645	54.02%	313	26.21%	2388	1117	46.78%	1271	53.22%	
105(1): 91-5.		GP														a
Michaelovsky E et al.																
Mol Psychiatry. 1999;	Israel	GP	454	-	117	25.77%	218	48.02%	119	26.21%	908	452	49.78%	456	50.22%	
4(1):97-9.																a
Osher Y et al. Mol																
Psychiatry 2000;	Israel	GP	148	51/97	39	26.35%	73	49.32%	36	24.32%	296	151	51.01%	145	48.99%	
5: 216-219.																a
		Aut/HRR														
Yirmiya N et al.																
Am J Med Genet. 2001;	Israel		66	-	15	22.73%	34	51.52%	17	25.76%	132	64	48.48%	68	51.52%	
105(4):381-6.		Control														a
TOTAL			2561		581	22.69%	1311	51.19%	669	26.12%	5122	2473	48.28%	2649	51.72%	
AVG						24.69%		49.15%		26.16%			49.26%		50.74%	

Borroni B et al. J Headache Pain. 2005; 6(4):182-4.		GP														
	Italy	(migraine)	249	51/198	53	21.29%	112	44.98%	84	33.73%	498	218	43.78%	280	56.22%	
																a
Monteleone P et al. Psychosom Med 2006; 68(1): 99-103.																
	Italy	BN/GP	219	0/219	63	28.77%	90	41.10%	66	30.14%	438	216	49.32%	222	50.68%	
																a
Nonnis Marzano F et al. Genomics. 2008; 91(6):485-91.		GP														
	Italy	(SIDS)	170	80/90	43	25.29%	94	55.29%	33	19.41%	340	180	52.94%	160	47.06%	
																b
Rotondo A et al. Am J Psychiatry. 2002; 159(1): 23-9.																
	Italy	BPD/GP	238	91/147	54	22.69%	121	50.84%	63	26.47%	476	229	48.11%	247	51.89%	
																a
TOTAL			876		213	24.32%	417	47.60%	246	28.08%	1752	843	48.12%	909	51.88%	
AVG						24.51%		48.05%		27.44%			48.54%		51.46%	
Katsuragi S et al. Biol Psychiatry 1999; 45: 368-370.																
	Japan	GP	101	62/39	66	65.35%	31	30.69%	4	3.96%	202	163	80.69%	39	19.31%	
																a
Kumakiri C et al. Neurosci Lett 1999; 263: 205-207.	Japan	GP	144	61/83	85	59.03%	48	33.33%	11	7.64%	288	218	75.69%	70	24.31%	
																a
Murakami F et al. J Hum Genet 1999; 44: 15-17.	Japan	GP	501	269/231	326	65.07%	159	31.74%	16	3.19%	1002	811	80.94%	191	19.06%	
																a
Nakamura K et al. Am J Med Genet Neuropsychiatr Genet 1997; 74: 544-545.																
	Japan	GP	186	0/186	128	68.82%	55	29.57%	3	1.61%	372	311	83.60%	61	16.40%	
																a
Umekage T et al. NeurosciLett 2003; 337: 13-16.																
	Japan	GP	244	54/190	161	65.98%	70	28.69%	13	5.33%	488	392	80.33%	96	19.67%	
																a
TOTAL			1176	446/729	766	65.14%	363	30.87%	47	4.00%	2352	1895	80.57%	457	19.43%	
AVG						64.85%		30.80%		4.35%			80.25%		19.75%	
THIS STUDY	Jordan	Moscow	18	-	4	22.22%	7	38,89%	7	38.89%	36	15	41.67%	21	58.33%	a
		students														

Ham BJ et al. Neurosci Lett 2004; 354(1): 2-5.	Korea	GP	146	47/99	93	63.70%	47	32.19%	6	4.11%	292	233	79.79%	59	20.21%	
																a
Joo YH et al. J Korean Med Sci 2007; 22(1): 138-141.	Korea	GP	158	69/89	95	60.13%	54	34.18%	9	5.70%	316	244	77.22%	72	22.78%	
																a
Kim SJ et al. J Neural Transm 2006; 113(7): 877-886	Korea	GP	209	101/108	128	61.24%	74	35.41%	7	3.35%	418	330	78.95%	88	21.05%	a
Kim SJ et al. Neuropsychobiology 2005; 51(4): 243-247.	Korea	GP	211	106/105	130	61.61%	72	34.12%	9	4.27%	422	332	78.67%	90	21.33%	
																a
Park JW et al. Headache 2004; 44(10): 1005-1009.	Korea	GP (CTH)	207	0/207	140	67.63%	62	29.95%	5	2.42%	414	342	82.61%	72	17.39%	a
TOTAL			931	323/608	586	62.94%	309	33.19%	36	3.87%	1862	1481	79.54%	381	20.46%	
AVG						62.86%		33.17%		3.97%			79.45%		20.55%	
Suriati et al. Asia-Pacific Psychiatry 2012; 4(2):126-130..	Malaysia	GP									66		22.00%		78.00%	
TOTAL													22.00%		78.00%	
AVG													22.00%		78.00%	
Camarena B et al. Int J Neuropsychopharmacol. 2001; 4(3):269-72.	Mexico	OCD/GP	251	-	76	30.28%	123	49.00%	52	20.72%	502	275	54.78%	227	45.22%	
																a
Cruz C et al. Arch Med Res 1995; 26: 421-426.	Mexico	Paper copy not availablc	72	-	20	27.78%	26	36.11%	26	36.11%	144	66	45.83%	78	54.17%	d
Lanzagorta N et al. Actas Esp Psiquiatr 2006; 34(5): 303-308.	Mexico	GP	57	25/32	21	36.84%	21	36.84%	15	26.32%	114	63	55.26%	51	44.74%	
																a
TOTAL			380	-	117	30.79%	170	44.74%	93	24.47%	760	404	53.16%	356	46.84%	
AVG						31.63%		40.65%		27.71%			51.96%		48.04%	
Nasserddine et al. Int J LifeSc Bt & Pharm Res 2012, 1: 278-281	Morocco	GP	100		20	20.00%	28	28.00%	52	52.00%	100	34	34.00%	66	66.00%	
TOTAL			100		20	20.00%	28	28.00%	52	52.00%	100	34	34.00%	66	66.00%	
AVG						20.00%		28.00%		52.00%			34.00%		66.00%	

Middeldorp CM et al. Behav Genet 2007; 37(2): 294-301.	Netherland	GP	989	-	195	19.72%	455	46.01%	339	34.28%	1978	845	42.72%	1133	57.28%	
														a		
TOTAL			989	-	195	19.72%	455	46.01%	339	34.28%	1978	845	42.72%	1133	57.28%	
Average						19.72%		46.01%		34.28%			42.72%		57.28%	
Caspi A et al. Science. 2003; 301 (5631): 386-9.	New Zealand	GP* (Health + Develop ment Study)	847	-	147	17.36%	435	51.36%	265	31.29%	1694	729	43.03%	965	56.97%	a
TOTAL			847	-	147	17.36%	435	51.36%	265	31.29%	1694	729	43.03%	965	56.97%	
AVG						17.36%		51.36%		31.29%			43.03%		56.97%	
THIS STUDY	Nigeria	Moscow students	37	-	3	8.11%	10	27.03%	24	64.86%	74	16	21.62%	58	78.38%	a
TOTAL			37	-	3	8.11%	10	27.03%	24	64.86%	74	16	21.62%	58	78.38%	
AVG			37	-	3	8.11%	10	27.03%	24	64.86%	74	16	21.62%	58	78.38%	
Landass et al. Journal of Affective Disorders 2011, 129: 308-312	Norway	GP	691		122	17.70%	328	47.50%	241	34.80%	691	287	41.50%	404	58.50%	
Jonassen et al. Frontiers in Human Neurosceience 2012, 6:1-5.	Norway	GP	33	0/33	12	36.36%	11	33.33%	10	30.30%						
TOTAL			724		134	18.50%	339	46.82%	251	34.67%	691	287	41.50%	404	58.50%	
AVG						27.03%		40.42%		32.55%			41.50%		58.50%	
Dragan WL, Oniszczɴko W. Neuropsychobiology 2006; 54(1): 45-50.	Poland	GP	196	0/196	22	11.22%	74	37.76%	100	51.02%	392	118	30.10%	274	69.90%	a
Samochowiec J et al. Neuropsychobiology 2001; 43: 248-253.	Poland	GP	126	-	18	14.29%	67	53.17%	41	32.54%	252	103	40.87%	149	59.13%	a
Sieminska A et al. BMC Med Genet. 2008; 9:76.	Poland	GP	307	162/145	42	13.68%	136	44.30%	129	42.02%	614	220	35.83%	394	64.17%	a

TOTAL			629		82	13.04%	277	44.04%	270	42.93%	1258	441	35.06%	817	64.94%	
AVG						13,06%		45,08%		41,86%			35,60%		64,40%	
Li J et al. Am J Med Genet		GP														
B Neuropsychiatr Genet.	PR China	(parents	558	279/279	323	57.89%	201	36.02%	34	6.09%	1116	847	75.90%	269	24.10%	
2007; 144B(1): 14-9.		of ADHD														
		Kids)	a													
	PR China	SA/!	1110	-	592	53.33%	450	40.54%	68	6.13%	2220	1634	73.60%	586	26.40%	
Shen Y et al. Neurosci Lett.		Pt/GP	a													
2004;372(1-2):94-8.																
You JS et al. Psychiatr																
Genet. 2005;15(1):7-11.	PR China	GAD/GP	228	107/121	138	60.53%	71	31.14%	19	8.33%	456	347	76.10%	109	23.90%	
																a
TOTAL			1896		1053	55.54%	722	38.08%	121	6.38%	3792	2828	74.58%	964	25.42%	
AVG						57.25%		35.90%		6.85%			75.20%		24.80%	
Kumsta et al. J Child																
Psychology and Psychiatry	Romania	Adoptees	125		31	24.80%	59	47.20%	35	28.00%	250	121	48.40%	129	51.60%	
2010, 51: 755-762																
Miu et al.																
Genes, Brains, Behavior	Romania	GP	128								256	115	44.92%	141	55.08%	
2012;11(4):398-403																
TOTAL			253								506	236	46.64%	270	53.36%	
AVG													46.66%		53.34%	
Alfimova MV et al.																
Neurosci Behav Physiol.	Russia	GP	224	109/115	41	18.30%	98	43.75%	85	37.95%	448	180	40.18%	268	59.82%	a
2008; 38(3):253-8.																
Gaysina D et al.																
Neuropsychobiology.	Russia	SA/GP	388	181/207	85	21.91%	184	47.42%	119	30.67%	776	354	45.62%	422	54.38%	
2006;54(1):70-4.																a
Golimbet VE et al. Am J																
Med Genet B																
Neuropsychiatr Genet. 2004;	Russia	!Pt	260	160/100	59	22.69%	119	45.77%	82	31.54%	520	237	45.58%	283	54.42%	
126B(1):1-7.																a
Noskova et al. Prog																
Neuropsychopharmacol Biol	Russia	GP	498	238/260	99	19.88%	243	48.80%	156	31.33%	996	441	44.28%	555	55.72%	
Psychiatry. 2008;32(7):1735-9.																

TOTAL			1370		284	20.73%	644	47.01%	442	32.26%	2740	1212	44.23%	1528	55.77%	
AVG						20.70%		46.43%		32.87%			43.91%		56.09%	
Kolassa et al.																
J Clin Psychiatry	Rwanda	Genocide	408	-	16	3.92%	109	26.72%	283	69.36%	816	141	17.28%	675	82.72%	
2010, 71: 543-547		Survivors														
TOTAL			408		16	3.92%	109	26.72%	283	69.36%	816	141	17.28%	675	82.72%	
AVG						3.92%		26.72%		69.36%	816	141	17.28%	675	82.72%	
Chong SA et al.																
Am J Med Genet. 2000;	Singapore	SCZ	188	149/39	99	52.66%	70	37.23%	19	10.11%	376	268	71.28%	108	28.72%	
96(6):712-5.																a
Chong SA et al.																
Psychiatry Res. 2000;	Singapore	SCZ/GP	441	-	233	52.83%	162	36.73%	46	10.43%	882	628	71.20%	254	28.80%	
97(2-3):101-6.																a
TOTAL			629		332	52.78%	232	36.88%	65	10.33%	1258	896	71.22%	362	28.78%	
AVG						52.75%		36.98%		10.27%			71.24%		28.76%	
Pungercic G et al.																
Psychiatr Genet. 2006;	Slovenia	SV/GP	468	-	88	18.80%	222	47.44%	158	33.76%	936	398	42.52%	538	57.48%	
16(5):187-91.																a
TOTAL			468	-	88	18.80%	222	47.44%	158	33.76%	936	398	42.52%	538	57.48%	
AVG						18.80%		47.44%		33.76%			42.52%		57.48%	
	South															
Esau L et al.	Africa	GP	342	-	16	4.68%	116	33.92%	210	61.40%	684	148	21.64%	536	78.36%	
Neural Transm. 2008;																a
115(5): 755-60.																
	South															
Saunders CJ et al. Hum	Africa	GP	411	411/0	65	15.82%	212	51.58%	134	32.60%	822	342	41.61%	480	58.39%	
Mol Genet. 2006;		(Athletes)														
15(20):2980-7.																a
TOTAL			753	-	81	10.76%	328	43.56%	344	45.68%	1506	490	32.54%	1016	67.46%	
AVG						10.25%		42.75%		47.00%			31.62%		68.38%	

Arias B et al. J Clin Psychopharmacol. 2003; 23(6):563-7.	Spain	MDD/GP	294	114/180	65	22.11%	147	50.00%	82	27.89%	588	277	47.11%	311	52.89%	
																a
Cervilla JA et al. Am J Med Genet B Neuropsychiatr Genet. 2006;141B(8):912-7.	Spain	GP	737	208/529	178	24.15%	367	49.80%	192	26.05%	1474	723	49.05%	751	50.95%	
																a
Dorado P et al. Fundam Clin Pharmacol. 2007; 21(4):451-3.	Spain	MDD/GP	212	94/118	43	20.28%	111	52.36%	58	27.36%	424	197	46.46%	227	53.54%	
																a
Gutiérrez B et al. Hum Genet. 1998; 103(3): 319-22.	Spain	MDD/GP	153	-	31	20.26%	78	50.98%	44	28.76%	306	140	45.75%	166	54.25%	
																a
Martínez-Barrondo S et al. Actas Esp Psiquiatr. 2005; 33(4):210-5.	Spain	PanD/GP	266	-	54	20.30%	116	43.61%	96	36.09%	532	224	42.11%	308	57.89%	
																a
		BPD/UP														
Masoliver E et al. Psychiatr Genet. 2006; 16(1):25-9	Spain	D/ GP	288	-	72	25.00%	132	45.83%	84	29.17%	576	276	47.92%	300	52.08%	
																a
Saiz PA et al. Prog Neuropsychopharmacol Biol Psychiatry. 2008; 32(3):765-70.	Spain	OCD/!P	975	531/444	212	21.74%	486	49.85%	277	28.41%	1950	910	46.67%	1040	53.33%	
		t/GP														
																a
Sáiz PA et al. Prog Neuropsychopharmacol Biol Psychiatry. 2007; 31(3):741-5.	Spain	SCZ	227	137/90	59	25.99%	104	45.81%	64	28.19%	454	222	48.90%	232	51.10%	
																a
TOTAL			3152		714	22.65%	1541	48.89%	897	28.46%	6304	2969	47.10%	3335	52.90%	
AVG						22.48%		48.53%		28.99%			46.75%		53.25%	

Gustavsson JP et al. Am J Med Genet Neuropsychiatr Genet 1999; 88: 430-436.	Sweden	GP	305	163/142	57	18.69%	151	49.51%	97	31.80%	610	265	43.44%	345	56.56%	
																a
Melke J et al. Am J Med Genet Neuropsychiatr Genet 2001; 105: 458-463.	Sweden	GP	251	0/251	53	21.12%	105	41.83%	93	37.05%	502	211	42.03%	291	57.97%	
																a
Nilsson KW et al. Neurosci Lett 2007; 411(3): 233-237.	Sweden	GP	196	79/117	44	22.45%	90	45.92%	62	31.63%	392	178	45.41%	214	54.59%	
																ab
TOTAL			752	242/510	154	20.48%	346	46.01%	252	33.51%	1504	654	43.48%	850	56.52%	
Average						20.75%		45.75%		33.50%			43.63%		56.37%	
Tsai SJ et al. Psychiatr Genet 2002; 12:165-168.	Taiwan	GP	192	94/98	100	52.08%	71	36.98%	21	10.94%	384	271	70.57%	113	29.43%	
	(China)															a
TOTAL			192	94/98	100	52.08%	71	36.98%	21	10.94%	384	271	70.57%	113	29.43%	
AVG						52.08%		36.98%		10.94%			70.57%		29.43%	
Butovskaya et al. Behav Genet 2012, 42(4):647-62.	Tanzania	GP-Hadza	95	95/0	3	4.00%	34	36.00%	57	60.00%	190	40	21.00%	150	79.00%	a
THIS STUDY	Tanzania	Moscow students	42	-	2	4.76%	16	38.10%	24	57.14%	84	20	23.81%	64	76.19%	a
TOTAL			137		5		50	36.00%	81	60.00%	274	60	21.00%	214	79.00%	
AVG						4.38%		37.00%		58.57%			22.41%		77.59%	
Tencomnao et al Asian Biomedicine 2010, 4: 893-899	Thailand	GP	194		99	51.03%	70	36.08%	25	12.89%	388	268	69.07%	120	30.93%	
TOTAL			194		99	51.03%	70	36.08%	25	12.89%	388	268	69.07%	120	30.93%	
AVG						51.03%		36.08%		12.89%			69.07%		30.93%	
Lotrich et al Am J of Pharmacogenomics 2012, 16: 15-27	Trinidad	GP	169		16	9.50%	45	26.60%	108	63.90%	169	39	23.00%	130	77.00%	
TOTAL																
AVG																

Akcali A et al. Neurol India. 2008; 56(2): 156-60	Turkey	(control to CTH)	264	38/226	86	32.58%	120	45.45%	58	21.97%	528	292	55.30%	236	44.70%	a
Mergen H et al. Endocr J. 2007;54(1):89-94.	Turkey	GP	399	-	121	30.33%	184	46.12%	94	23.56%	798	426	53.38%	372	46.62%	a
Pata C et al. Am J Gastroenterol. 2002; 97(7):1780-4.	Turkey	GP	145	76/69	54	37.24%	62	42.76%	29	20.00%	290	170	58.62%	120	41.38%	a
Yilmaz M et al. J Neurol Sci. 2001; 186(1-2):27-30	Turkey	GP (control to migraine)	132	-	37	28.03%	54	40.91%	41	31.06%	264	128	48.48%	136	51.52%	a
Zorolu SS et al. Neuropsychobiology. 2002;45(4):176-81.	Turkey	ADHD/ GP	190	-	57	30.00%	87	45.79%	46	24.21%	380	201	52.89%	179	47.11%	a
TOTAL			1130		355	31.42%	507	44.87%	268	23.71%	2260	1217	53.85%S	1043	46.15%	
AVG						39.55%		55.26%		30.20%			53.73%		46.27%	
Deary IJ et al. Psychol Med 1999; 29: 735-739.	UK	GP	204	-	43	21.08%	101	49.51%	60	29.41%	408	187	45.83%	221	54.17%	a
Munafo MR et al. Neuropsychobiology 2006; 53(1): 1-8.	UK	GP	251	85/166	46	18.33%	129	51.39%	76	30.28%	502	221	44.02%	281	55.98%	a
Willis-Owen SA et al. Biol Psychiatry 2005; 58(6): 451-456	UK	GP	5433	-	981	18.06%	2610	48.04%	1842	33.90%	10866	4572	42.08%	6294	57.92%	a
TOTAL			5888	-	1070	18.17%	2840	48.23%	1978	33.59%	11776	4980	42.29%	6796	57.71%	
AVG						19.15%		49.65%		31.20%			43.98%		56.02%	
THIS STUDY	Ukraine	GP	41	-	11	26.83%	15	36.59%	15	36.59%	82	37	45.12%	45	54.89%	a
TOTAL			41	-	11	26.83%	15	36.59%	15	36.59%	82	37	45.12%	45	54.89%	
AVG					11	26.83%	15	36.59%	15	36.59%	82	37	45.12%	45	54.89%	

Genotyping Method:
a. PCR/Gel Electrophoresis, b. PCR/Sequencing, c. PCR/Gel Microchip Electrophoresis, d. Paper Not Available

Population and DNA samples analyzed in this study.

Buccal swabs or blood samples were collected from Moscow students or from general population (Ukraine). Samples were obtained and analyzed after advice of the IRB of Institute of General Genetics RAS in accordance with the declaration of Helsinki. Anonymous ID numbers were applied to the DNA samples in order to provide the confidentiality of all subjects. DNA was isolated by standard protocols. Primers and PCR conditions used to analyze HTTLPR polymorphism are available by request. This part of the study is supported by RFBR 10-04-01802.

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Willeit M et al. (2003), *Mol Psychiatry* 8(11): 942–6.
Willis-Owen SA et al. (2005), *Biol Psychiatry* 58(6): 451–456.
Yilmaz M et al. (2001), *J Neurol Sci*. 186(1/2): 27–30.
Yirmiya N et al. (2001), *Am J Med Genet*. 105(4): 381–6.
You JS et al. (2005), *Psychiatr Genet*. 15(1): 7–11.
Zorolu SS et al. (2002), *Neuropsychobiology* 45(4): 176–81.

Table A2 *COMT Val158Met* genotype and allele frequencies in studied countries

Journal	Country /Continent	SubPop	Pop	n-Genotype	met/met (A/A)	met/val (A/G)	val/val (G/G)	n-Allele	%Met (A)	%Val (G)	Genotyping Method
Li et al. Science. 2008. 319:1100-1104.	Algeria	Mozabite						60	42.00	58.00	
TOTAL								60	42.00	58.00	
AVERAGE									42.00	58.00	
Olsson et al. Psychiatric Genetics. 2005, 15: 109-115.	Australia		GP	2032	27.00	50.00	23.00	4064	52.0	48.00	hME
TOTAL				2032	27.00	50.00	23.00	4064	52.0	48.00	
AVERAGE					27.00	50.00	23.00	4064	52.0	48.00	
Weiss et al. Journal of International Nueropsychological Society. 2007, 13: 881-887.	Austria		GP	100	17.00	58.00	25.00	200	46.00	54.00	PCR
Defrancesco et al. Journal of the International Neuropsychological Society. 2011, 17: 1014-1020.	Austria		GP	88	20.45	48.86	30.68	176	44.88	55.12	PCR
TOTAL				188	18.62	53.72	27.66	376	45.48	55.52	
AVERAGE					18.73	53.43	27.84		45.44	54.56	
THIS STUDY	Belarus	Belarussians	GP	60	23.33	48.33	28.33	120	47.50	52.50	PCR
TOTAL								120	47.50	52.50	
AVERAGE								120	47.50	52.50	

Simons et al. Genes, Brains and Behavior. 2009, 8: 5-12.	Belgium		GP	461	21.80	53.70	24.50	922	48.65	51.35	KBioscience
TOTAL								922	48.65	51.35	
AVERAGE								922	48.65	51.35	
Galvao et al. Journal of Nutritional Biochemistry. 2012, 23: 272-277.	Brazil		GP	326	37.70	47.50	14.80	654	61.50	38.50	PCR
Almeida et al. The Pharmacogenetics Journal. 2005, 5: 346-351.	Brazil	European	GP-Female	212				424	45.00	55.00	
Valente et al. J Mol Neurosci. 2011, 43: 516-523.	Brazil		GP	335	7.76	55.22	37.02	670	35.37	64.63	PCR
TOTAL								1748	47.48	52.52	
AVERAGE									47.29	52.71	
Potvin et al. J Pain. 2009, 10: 969-975.	Canada		GP	36	16.67	58.33	25.00	72	45.83	54.17	Not stated
Onay et al. BMC Cancer 2008, 8:6	Canada		GP-Female	714	22.41	49.44	28.15	1428	47.13	52.87	
Sheikh et al., Am J Med Genet B Neuropsychiatr Genet. 2013, 162: 245-252.	Canada		GP, 90.5% Caucasian	401	23.19	47.38	29.43	802	46.88	53.12	
TOTAL								2302	47.00	53.00	
AVERAGE									46.61	53.39	
Liang et al. Archives of Medical Research. 2012, 43: 154-158.	China		GP	189	4.80	32.80	62.40	378	21.20	78.80	PCR
Chen et al. Neuropsycho-pharmacology. 2011, 36: 1593-1598.	China		GP	556	6.47	37.77	55.76	1112	25.55	74.45	PCR
Wang et al. DNA and Cell Biology. 2011, 30: 585-595.	China		GP Female	400	9.00	39.00	52.00	800	28.50	71.50	PCR-RFLP

Yu et al. Am J Med Genet. Part B 2007;144:570e3.	China		GP	115	4.35	37.39	58.26	230	23.04	76.96	PCR
TOTAL				1580	11.39	39.75	48.86	2520	25.60	74.40	
AVERAGE					10.80	39.19	50.00		24.66	75.34	
Forero et al. Neurosci. Res. 2006, 55: 334-341.	Colombia		Control to Alzheimer Disease	161	32.90	55.90	11.20	322	60.90	39.10	PCR
TOTAL				161	32.90	55.90	11.20	322	60.90	39.10	
AVERAGE					32.90	55.90	11.20	322	60.90	39.10	
Nedic et al. Neurosci. Lett.. 2010, 473: 216-219.	Croatia		GP	657	23.74	50.08	26.18	1314	48.78	51.22	PCR
TOTAL								1314	48.78	51.22	
AVERAGE								1314	48.78	51.22	
Serý et al. Neuro Endocrinol Lett. 2006, 27 (1-2):231-235.	Czech Republic	Czech	GP	400	26.00	50.75	23.25	800	51.4	48.6	PCR-RFLP
TOTAL								800	51.4	48.6	
AVERAGE								800	51.4	48.6	
Kring et al. PLoS One. 2009; 4(8):e6696.	Denmark	Danes	GP	271	29.52	52.40	18.08	542	55.72	44.28	Taqman (Kbioscience)
Palmatier et al. Mol Psychiatry. 2004:9:859-70.*	Denmark	Danes	GP	61				102	60.80	39.20	
TOTAL								644	56.52	43.48	

AVERAGE									58.26	42.72	
Wolpert. Dissertation, University of Maryland Baltimore. 2009: online.	Egypt		GP	420	23.81	46.43	29.76	840	52.98	47.02	Real-time PCR
TOTAL				420	23.81	46.43	29.76		52.98	47.02	
AVERAGE				420	23.81	46.43	29.76		52.98	47.02	
Maron et al. Neurosci Lett. 2008, 446: 88-92.	Estonia		GP	110	28.30	55.80	15.90	220	56.20	43.80	Not stated
Nelis et al. PLoS One. 2009, 4: e5472. *	Estonia		GP	976				1952	57.20	42.80	
TOTAL								2172	57.14	42.86	
AVERAGE									56.70	42.30	
DeMille et al. Human Genetics. 2002, 111:521-537.*	Ethiopia	Jews						64	32.80	67.20	
TOTAL								64	32.80	67.20	
AVERAGE								64	32.80	67.20	
Salo et al. Psychiatric Genetics. 2010, 20: 273-281.	Finland		GP	1214	28.20	50.10	21.70	2428	53.25	46.75	PCR
Kauhanen et al. Alcohol Clin Exp Res. 2000:24(2):135-139.	Finland			896	30.02	47.77	22.21	1792	53.90	46.10	PCR-RFLP
Voutilainen et al. PLoS One. 2007: 1;2(1):e181.	Finland			792	28.94	49.37	21.72	1584	53.60	46.40	PCR-RFL
TOTAL								5804	53.55	46.45	
AVERAGE									53.58	46.42	
Saintot et al. Int J Cancer. 2003, 107: 652-657.	France		GP - Female	282	19.50	49.65	30.85	2428	53.25	55.68	PCR-RFLP

Delort et al. Nutr Cancer. 2010, 62:243–251	France		GP - Female	1000	28.30	48.00	23.70	1792	53.90	47.70	
TOTAL								1584	53.60	46.40	
AVERAGE									48.31	51.69	
Osinsky et al. Brain Research. 2012, 1452: 108-118.	Germany		GP	65	35.38	38.46	26.15	130	54.61	45.39	N400
Domschke et al. NeuroImage. 2012, 60: 2222-2229.	Germany		GP	85	30.89	49.41	20.00	170	55.60	44.40	iPLEX
Wacker and Mueller. J Pers Soc Psychol.. 2012, 102: 427-444.	Germany		GP-Male	201	30.85	50.25	18.91	402	55.98	44.03	Not stated
Brandys et al. Psychiatr Genet. 2012, 22: 130-136.	Germany		GP	96	32.30	46.90	20.80	192	55.70	44.30	Not stated
TOTAL				447	31.76	47.65	20.59	894	55.65	44.35	
AVERAGE					32.36	46.26	21.47		55.47	44.53	
Ameyaw et al. Hum Mutat. 2000, 16: 445-446. *	Ghana	Ewe						64	30.00	70.00	
Ameyaw et al. Hum Mutat. 2000, 16: 445-446. *	Ghana	Fanti						74	23.00	77.00	
Ameyaw et al. Hum Mutat. 2000, 16: 445-446. *	Ghana	Ga						92	20.00	80.00	
Ameyaw et al. Hum Mutat. 2000, 16: 445-446. *	Ghana	GP						390	26.00	74.00	
TOTAL								620	25.00	75.00	
AVERAGE									24.75	75.25	
Kalinderi et al. Eur J Neurol. 2008, 15: e83.	Greece		GP	125	28.80	39.20	32.00	500	48.40	51.60	Not stated
Roussos et al. Psychological Medicine. 2008, 38: 1651-1658.	Greece		GP	93	16.13	51.61	32.26	186	41.94	58.06	PCR-RFLP

Stefanis et al. American Journal of Psychiatry. 2005, 162: 1752-1754.	Greece		GP- Male	543	20.60	46.00	33.00	1086	43.60	56.40	PCR
TOTAL								1772	xx	xx	
AVERAGE									44.65	55.35	
Demetrovics et al. Comprehensive Psychiatry. 2010, 51: 510-515.	Hungary		GP	124	25.80	48.40	25.80	248	50.00	50.00	PCR
Kerezturi et al. Am J Med Genet. Part B. 2008, 147B: 1431-1435.	Hungary		GP	284	28.17	53.17	18.66	568	54.76	45.24	Not stated
Mukherjee et al. Molecular Psychiatry. 2010: 15:216-225*.	Hungary							174	56.30	43.70	
TOTAL								990	xx	xx	
AVERAGE									53.69	46.31	
Haraldsson et al. Schizophrenia Bulletin. 2010, 36: 157-167.	Iceland		GP	95	31.58	54.74	13.68	190	58.95	41.05	Not stated
TOTAL				95	31.58	54.74	13.68	190	58.95	41.05	
AVERAGE					31.58	54.74	13.68	190	58.95	41.05	
Das et al. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2011, 35: 577-587.	India		GP	96				192	43.30	56.70	PCR
Gupta et al. Pharmacogenomics. 2009, 10(3):385-97	India		GP	239	17.15	53.56	29.29	478	43.93	56.07	
Syamala et al. Cancer Investigation. 2010, 28: 304-311.	India		GP	367	17.70	44.70	37.60	734	40.12	59.78	PCR-RFLP
TOTAL								1404	44.78	55.22	
AVERAGE									42.45	57.55	

Omrani et al. J Res Med Sci. 2009, 14: 217-222.	Iran		GP - Male	107	1.86	93.45	4.67	214	48.50	51.40	Not stated
TOTAL				107	1.86	93.45	4.67	214	48.50	51.40	
AVERAGE					1.86	93.45	4.67		48.50	51.40	
Williams et al. Am J Psychiatry. 2005.162:1736-8.	Ireland			961	23.93	46.72	29.34	1922	47.29	52.71	
Palmatier et al. Mol Psychiatry. 2004 9: 859-70.*	Ireland							230	50.00	50.00	
TOTAL				61	15.00	62.00	23.00				
AVERAGE					15.00	62.00	23.00	2252	48.65	51.35	
Poyurovsky et al. Neurosci. Lett. 2005, 389: 21-24.	Israel		GP	171	20.00	52.00	28.00	342	46.00	54.00	Not stated
Mukherjee et al. Molecular Psychiatry. 2010: 15:216-225*.	Israel	Ashkenazi						146	48.60	51.40	
TOTAL				171	20.00	52.00	28.00	488	46.78	53.22	
AVERAGE					20.00	52.00	28.00		47.30	52.70	
Nobile et al. Eur Child Adolesc Psychiatry. 2010, 19: 549-557.	Italy		GP	575	22.60	48.00	29.40	575	46.60	53.40	Taqman Assay
Rotondo et al. American Journal of Psychiatry. 2002, 159: 23-29.	Italy		GP	127	15.00	48.00	37.00	254	39.00	61.00	PCR
Brandys et al. Psychiatr Genet. 2012, 22: 130-136.	Italy		GP	83	20.50	53.00	26.50	166	47.00	53.00	Not stated
Brandys et al. Psychiatr Genet. 2012, 22: 130-136.	Italy		GP	146	27.40	43.10	29.50	292	49.00	51.00	Not stated
TOTAL				964	21.99	48.13	29.88	1287	45.70	54.30	

AVERAGE					20.74	50.54	28.72		45.40	54.60	
Hiyoshi et al. Gene. 2012, 496: 97-102.	Japan		GP	1808	13.16	45.13	41.70	3616	35.73	64.27	Invader Assay
Htun et al. Am J Hypertens. 2011, 24: 1022-1026.	Japan		GP - Male	735	10.61	40.82	48.57	1470	31.02	68.98	PCR
Nunokawa et al. Neurposci. Res. 2007, 58: 291-296.	Japan		GP	440	10.90	40.00	49.09	880	30.90	69.10	PCR
TOTAL				2983				5966	33.86	66.14	
AVERAGE									32.55	67.45	
THIS STUDY	Jordan		GP	21	38.10	33.33	28.57	42	54.76	45.24	Real-time PCR
TOTAL								42	54.76	45.24	
AVERAGE								42	54.76	45.24	
Lee and Kim. Neuropsychobiology. 2011, 63: 177-182.	Korea, South		GP	170	9.41	50.00	40.59	340	34.41	65.59	PCR
Yim et al. Pharmacogenetics. 2001, 11:279–286	Korea, South		GP-Female	163	9.82	28.22	61.96	326	23.93	76.07	
Kang Epidemiol Health. 2010, 32:e2010011.	Korea, South		GP	348	6.90	37.90	55.20	696	25.28	74.2	PCR
TOTAL				843	8.07	42.35	49.58	1362	27.23	72.77	
AVERAGE					8.38	43.63	48.00		27.88	72.12	
Mukherjee et al. Molecular Psychiatry. 2010: 15:216-225. *	Laos	Lao Loum		113				226	22.10	77.90	
TOTAL								226	22.10	77.90	
AVERAGE									22.10	77.90	

Wan et al. Psychiatry Research. 2011. 189: 67-71.	Malaysia		GP	417	9.35	36.21	54.44	834	72.54	27.46	PCR
TOTAL				417	9.35	36.21	54.44	834	72.54	27.46	
AVERAGE					9.35	36.21	54.44		72.54	27.46	
Tovilla-Zarate et al. BMC Psychiatry. 2011, 11: 151-158.	Mexico		GP	236	15.70	47.60	33.20	472	39.50	60.50	PCR
TOTAL								472	39.50	60.50	
AVERAGE								472	39.50	60.50	
Brandys et al. Psychiatr Genet. 2012, 22: 130-136.	Netherlands		GP	466	32.20	50.00	17.80	932	57.20	42.80	MASS Array
Katerberg et al. Am J Med Genet Part B 153B:167–176	Netherlands		GP	462	26.41	49.35	24.24	924	51.09	48.91	
Stolk et al. J Clin Endocrinol Metab. 2007, 92(8):3206–3212	Netherlands		GP	6069	29.86	49.45	20.69	12138	54.85	45.15	
TOTAL								13944	54.95	45.05	
AVERAGE									54.19	45.81	
Caspi et al. Biol Psychiatry. 2005, 57: 1117-1127.	New Zealand		GP	803	25.00	50.00	25.00	1606	50.00	50.00	PCR
TOTAL					25.00	50.00	25.00		50.00	50.00	
AVERAGE					25.00	50.00	25.00		50.00	50.00	
DeMille et al., Human Genetics. 2002: 111: 521-537.*	Nigeria	Hausa						76	26.30	73.70	
DeMille et al., Human Genetics. 2002: 111: 521-537.*	Nigeria	Ibo						96	26.50	63.50	
Palmatier et al. Mol Psychiatry. 2004. 9:859-870. *	Nigeria	Yoruba						138	34.80	65.20	

TOTAL								310			
AVERAGE									29.20	70.80	
Baekken et al. BMC Psychiatry. 2008, 8: 48-55.	Norway		GP	5531	31.98	49.29	18.73	11062	56.63	43.37	PCR
Hagen et al. Pharmacoepidemiology and Drug Safety. 2008, 17: 372-377.	Norway		GP	2623	31.72	49.56	18.72	5246	56.50	43.50	Not stated
TOTAL				8154	31.90	49.37	18.73	16308	56.59	43.41	
AVERAGE					31.85	49.43	18.73		56.56	43.44	
Li et al. Science. 2008, 319:1100-1104.*	Pakistan	Burusho						50	48.00	52.00	Illumina HumanHap650K Beadchip
Li et al. Science. 2008, 319:1100-1104.*	Pakistan	Kalash						50	54.00	46.00	Illumina
Li et al. Science. 2008, 319:1100-1104.*	Pakistan	Balochi						50	54.00	46.00	Illumina
Li et al. Science. 2008, 319:1100-1104.*	Pakistan	Brahui						50	42.00	58.00	Illumina
Li et al. Science. 2008, 319:1100-1104.*	Pakistan	Hazara						48	52.00	48.00	Illumina
Li et al. Science. 2008, 319:1100-1104.*	Pakistan	Sindhi						50	42.00	58.00	Illumina
TOTAL								298	48.64	51.36	
AVERAGE									48.67	51.33	
Huerta et al. An Fac Med Lima. 2007, 68: 321-327.	Peru		GP	106	7.00	51.00	42.00	106	32.00	68.00	PCR-RFLP
TOTAL				106	7.00	51.00	42.00	106	32.00	68.00	

AVERAGE					7.00	51.00	42.00	106	32.00	68.00	
Baclig et al. Int Mol Epidemiol Genet. 2012, 3: 115-121.	Philippines		GP	95	1.05	31.58	67.37	190	16.84	83.16	PCR
TOTAL				95	1.05	31.58	67.37	190	16.84	83.16	
AVERAGE					1.05	31.58	67.37	190	16.84	83.16	
Pelka-Wysieka et al. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2012: online.	Poland		GP	406	25.25	60.54	14.22	406	55.52	44.48	Not stated
Gaudet et al. Cancer Res. 2006, 66:9781–9785**	Poland		GP-female	2279	23.65	49.28	27.07	4558	48.29	51.72	
Samochowiec et al. Psychiatry Research. 2004, 128: 21-26.	Poland		GP	197	28.00	48.00	24.00	394	52.00	48.00	Not stated
TOTAL								5358	49.11	50.89	
AVERAGE									51.94	48.06	
Drury et al. Child Abuse and Neglect. 2010, 34: 387-395.	Romania		Orphans	98	13.27	52.04	34.69	98	39.00	61.00	PCR
TOTAL				98	13.27	52.04	34.69	98	39.00	61.00	
AVERAGE					13.27	52.04	34.69		39.00	61.00	
Palmatier et al. Biol Psychiatry. 1999, 46: 557-567. *	Russia	Russians	Vologda region	48	31.25	39.58	29.17	96	51.00	49.00	
Salnikova et al. Technology of Life Systems. 2009, 6 (4): 42-49.	Russia	Russians	Tula and Briansk region	108	29.63	51.85	18.52	216	55.56	44.44	
Golimbet et al., World J Biol Psychiatry. 2006;7(4):238-45.	Russia	Russians	Moscow	130	22.31	51.54	26.15	260	48.08	51.92	
THIS STUDY	Russia	Russians	St. Petersburg	487	29.98	47.64	22.38	974	53.80	46.20	PCR

TOTAL								1546	52.91	47.09	
AVERAGE									52.11	47.89	
Kolassa et al. Biol Psychiatry. 2010, 67: 304-308.	Rwanda		Genocide Survivors	424	10.85	44.81	44.34	848	33.25	66.75	Not stated
TOTAL				424	10.85	44.81	44.34	848	33.25	66.75	
AVERAGE					10.85	44.81	44.34	848	33.25	66.75	
Lim et al. PLoS One. 2012;7(3):e33767.	Singapore		GP	324	6.20	37.30	56.50	648	24.80	75.20	MASS Array
TOTAL				324	6.20	37.30	56.50	648	24.80	75.20	
AVERAGE					6.20	37.30	56.50		24.80	75.20	
Cerne et al. J Gynecol Oncol. 2011, 22:110–119	Slovenia		GP	270	24.81	50.37	24.81	540	50.00	50.00	Taqman Assay
Pivac et al. Genes Brain Behav. 2011, 10: 565-569.	Slovenia		GP	198	28.28	48.99	22.73	396	52.78	47.22	Taqman Assay
TOTAL				468	26.28	49.79	23.93	936	51.18	48.82	
AVERAGE					24.81	49.68	23.77		51.39	48.61	
Lochner et al. J Clin Psychiatry.2005, 66: 1155-1160.	South Africa		GP - Caucasian	81	16.05	61.73	22.22	162	46.91	53.09	Not stated
TOTAL				81	16.05	61.73	22.22	162	46.91	53.09	
AVERAGE					16.05	61.73	22.22	162	46.91	53.09	
Brandys et al. Psychiatr Genet. 2012, 22: 130-136.	Spain		GP	93	24.70	47.30	28.00	186	48.40	51.60	Not stated
Martorell et al. Schizophr Res. 2008, 100:308-315.	Spain		GP	615				1230	43.30	56.70	

Hoenicka et al. Am J Med Genet. Part B. 2010;153:79e85	Spain			285	24.56	48.42	27.02	570	48.77	51.23	
Costas et al. Journal of Psychiatric Research. 2011, 45: 7-14.	Spain		GP	1025	18.73	51.51	29.76	2050	44.49	55.51	MASS Array
TOTAL				1264	20.09	50.63	29.28	552	44.20	55.80	
AVERAGE					23.82	48.23	27.95		44.13	55.87	
Karling et al. PLoS One. 2011, 6:	Sweden		GP	867	31.00	49.00	20.00	2734	55.00	45.00	PCR
Comasco et al. Psychiatr Genet. 2011, 21: 19-28.	Sweden		GP - Female	272	27.60	48.90	23.50	272	52.00	48.00	Not stated
Aberg et al. Journal of Affective Disorders. 2011, 129: 158-166.	Sweden		GP	2151	30.45	49.00	20.55	4302	54.95	45.05	Not stated
Lorentzon et al. J J Bone Miner Res.. 2004, 19: 2005-2011.	Sweden		GP - Male	458	30.35	51.31	18.34	916	56.00	44.00	PCR
TOTAL				3748	30.34	49.28	20.38	82.24	54.99	55.01	
AVERAGE					29.85	49.55	20.60		54.49	45.51	
Desmeules et al. Health Psychology. 2012, 31: 242-249.	Switzerland		GP	99	25.30	44.40	30.30	198	47.50	52.50	PCR
Baud et al. Am J Med Genet Part B. 2007, 144B: 1042-1047.	Switzerland		GP	185	23.80	57.80	18.40	370	52.70	47.30	PCR
TOTAL				284	24.30	53.17	22.53	568	50.88	49.12	
AVERAGE					24.55	51.10	24.35		50.10	49.90	
Palmatier et al. Biol Psychiatry. 1999, 46: 557-567.*.	Taiwan	Han						100	26.00	74.00	
Liou et al. Neuropsychobiology. 2001, 43: 11-4.*	Taiwan	Han						376	26.90	73.10	

Chen et al. Am J Med Genet. 1996, 67: 556-559*.	Taiwan	Han						198	27.00	73.00	
DeMille et al. Human Genetics. 2002, 111:521-537.*.	Taiwan	Hakka						84	16.70	83.30	
TOTAL								758	25.68	74.32	
AVERAGE									24.15	75.85	
Palmatier et al. Mol Psychiatry. 2004: 9:859-70.*	Tanzania	Chagga						90	27.80	72.20	
TOTAL								90	27.80	72.20	
AVERAGE								90	27.80	72.20	
Sangrajrang et al. Int J Cancer. 2009, 125:837–843.	Thailand			486	6.00	39.00	55.00	486	25.50	74.50	Taqman Assay
TOTAL				486	6.00	39.00	55.00	486	25.50	74.50	
AVERAGE					6.00	39.00	55.00	486	25.50	74.50	
Karacetin et al. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2012, 36: 5-10.	Turkey		GP	130	20.80	66.90	12.30	130	54.20	45.80	PCR
Baransel Isir et al. Am J Forensic Med Pathol. 2008, 29: 320-322.	Turkey		GP	75	13.30	58.70	28.00	75	42.70	57.30	Not stated
Kocabas et al. Arch Toxicol. 2001, 75: 407-409.*	Turkey							434	45.00	55.00	
TOTAL				205	18.05	63.90	18.05	639	46.48	53.52	
AVERAGE					17.05	62.80	20.15		47.30	52.70	
Dunning et al. J Natl Cancer Inst. 2004, 96:936–994	United Kingdom		GP Female	1908	27.99	48.53	23.48	3816	52.26	47.74	

Shaikh et al. Psychological Medicine. 2011, 41: 263-276.	United Kingdom		GP	192	25.52	51.56	22.92	384	51.30	48.70	Taqman Assay
Yue et al. NueroReport. 2009, 20: 521-524.	United Kingdom		GP	78	32.05	42.31	25.64	156	53.21	46.79	Not stated
TOTAL				299	28.76	48.16	23.08	4356	52.26	47.74	
AVERAGE					32.98	45.08	21.93				
THIS STUDY	Ukraine	Ukrainian	GP	73	26.03	43.83	30.14	146	47.95	52.05	
TOTAL								146	47.95	52.05	
AVERAGE								146	47.95	52.05	

* ALFRED populations

** He et al. (2012), *Mol Biol Rep*. 39: 6811–6823.

Population and DNA samples analyzed in this study

Buccal swabs or blood samples were collected from Moscow students. Samples were obtained and analyzed after advice of the IRB of Institute of General Genetics RAS in accordance with the declaration of Helsinki. Anonymous ID numbers were applied to the DNA samples in order to provide the confidentiality of all subjects. DNA was isolated by standard protocols. Primers and PCR conditions used to analyze COMT Val158Met (rs4680) polymorphism are available by request. This study was partially supported by RFBR 10-04-01802.

Allele Frequency DataBase (ALFRED) was used as a source of *COMT Val158Met* (rs4680) allele frequency data for 29 populations. We searched for additional studies using PubMed with request COMT + country name. 3–4 articles with biggest sample size were selected when available. In case of articles with sample overlap those with low sample size were excluded. Samples which were not in HWE were excluded.

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Table A3 STR allele frequencies

D8_8	D8_9	D8_10	D8_11	D8_12	D8_13	D8_14	D8_15	D8_16	D8_17	D8_18	D8_19
0	0	0,205	0,034	0,08	0,148	0,25	0,25	0,034	0	0	0
0,011	0,017	0,083	0,076	0,161	0,317	0,193	0,115	0,023	0,004	0,001	0
0	0,011	0,033	0,109	0,196	0,337	0,196	0,054	0,043	0,022	0	0
0,02	0,005	0,083	0,077	0,135	0,309	0,241	0,099	0,032	0	0	0
0,005	0,01	0,105	0,06	0,185	0,255	0,25	0,11	0,02	0	0	0
0,0207	0,0145	0,0971	0,1054	0,1302	0,3161	0,1921	0,093	0,0248	0,0062	0	0
0	0	0,141	0,113	0,133	0,222	0,168	0,16	0,051	0,008	0,004	0
0,006	0,01	0,063	0,083	0,128	0,332	0,231	0,116	0,029	0,003	0	0
0	0	0	0	0	0	0	0	0	0	0	0
0,007	0,01	0,087	0,062	0,152	0,341	0,221	0,112	0,005	0,0003	0	0
0,015	0,006	0,057	0,108	0,111	0,208	0,242	0,191	0,046	0,011	0,004	0
0,014	0,008	0,05	0,078	0,169	0,433	0,169	0,056	0,014	0,008	0	0
0,017	0,011	0,086	0,078	0,137	0,321	0,213	0,095	0,036	0,005	0,001	0
0	0	2	0,022	0,037	0,134	0,187	0,303	0,216	0,08	0,017	0
0,021	0,004	0,095	0,063	0,112	0,311	0,217	0,136	0,032	0,007	0,004	0
0,0145	0,0123	0,0624	0,0761	0,1516	0,3107	0,2211	0,1187	0,0287	0,0031	0,0005	0
0,013	0,023	0,07	0,073	0,149	0,268	0,275	0,113	0,017	0	0	0
0,011	0	0,158	0,066	0,095	0,138	0,198	0,21	0,106	0,011	0,006	0
0,0067	0,02	0,0867	0,06	0,1333	0,3067	0,1633	0,1467	0,06	0,0167	0	0

0,022	0,014	0,074	0,083	0,114	0,306	0,206	0,143	0,034	0,003	0	0
0	0,005	0,144	0,071	0,12	0,235	0,222	0,135	0,063	0,006	0	0
0,005	0,005	0,005	0,068	0,132	0,253	0,237	0,232	0,042	0,016	0,005	0
0	0	0,089	0,086	0,104	0,208	0,239	0,173	0,081	0,015	0,005	0
0	0,004	0,021	0,03	0,118	0,19	0,35	0,197	0,068	0,017	0,004	0
0,01	0,008	0,083	0,076	0,135	0,338	0,23	0,096	0,022	0,002	0	0
0,015	0,003	0,159	0,067	0,086	0,196	0,164	0,208	0,093	0,005	0,005	0
0,01	0,009	0,069	0,067	0,166	0,339	0,218	0,094	0,023	0,005	0	0
0,024	0,014	0,053	0,087	0,139	0,356	0,197	0,087	0,038	0,005	0	0
0,005	0,005	0,063	0,08	0,193	0,332	0,192	0,096	0,028	0,005	0	0
0	0	0,0192	0,0577	0,1538	0,1538	0,2692	0,2788	0,0385	0,0288	0	0
0,004	0,002	0,116	0,087	0,15	0,251	0,166	0,152	0,062	0,01	0	0
0,0047	0,0047	0,0623	0,0592	0,1682	0,3115	0,2414	0,1231	0,0234	0,0016	0	0
0,016	0,0068	0,105	0,0822	0,1416	0,2717	0,226	0,1164	0,032	0,0023	0	0
0,008	0,012	0,098	0,068	0,159	0,332	0,188	0,112	0,019	0,003	0	0
0,0146	0,0073	0,0947	0,0947	0,1335	0,2694	0,2087	0,1359	0,0364	0,0049	0	0
0	0	0,0289	0,0549	0,1329	0,1561	0,3237	0,2023	0,1012	0	0	0
0,005	0	0,149	0,097	0,105	0,153	0,193	0,195	0,078	0,023	0,003	0
0,023	0,019	0,061	0,06	0,111	0,258	0,247	0,171	0,042	0,008	0	0
0,0108696	0,0072464	0,0507246	0,076087	0,1557971	0,3152174	0,2427536	0,115942	0,0217391	0,0036232	0	0

Forensic STR allele frequency tables were downloaded from Database for autosomal short tandem repeats (http://allstr.de) and ALFRED database (http://alfred.med.yale.edu/alfred/)

Data for the following countries were added.

Country	Reference			Comments
Algeria	Bosch E, Clarimón J, Pérez-Lezaun A, Calafell F.	STR data for 21 loci in northwestern Africa.	Forensic Sci Int. 2001 Feb 1;116(1):41-51.	Algeria: data for Mozabites
Bangladesh	Ferdous A, Ali ME, Alam S, Hasan M, Hossain T, Akhteruzzaman S.	Forensic evaluation of STR data for the PowerPlex 16 System loci in a Bangladeshi population.	Leg Med (Tokyo). 2009 Jul;11(4):198-9	
Belarus	Stepanov V.A. et al.,	Characteristics of Populations of the Russian Federation over the Panel of Fifteen Loci Used for DNA Identification and in Forensic Medical Examination.	Acta Naturae. 2011. Т. 3. № 2 (9). С. 59-71. (in Russian)	All regions of Belarus
Britain	Tucker VC, Hopwood AJ, Sprecher CJ, McLaren RS, Rabbach DR, Ensenberger MG, Thompson JM, Storts DR.	Developmental validation of the PowerPlex(®) ESI 16 and PowerPlex(®) ESI 17 Systems: STR multiplexes for the new European standard.	Forensic Sci Int Genet. 2011 Nov;5(5):436-48.	
Czech Rep.	Simková H, Faltus V, Marvan R, Pexa T, Stenzl V, Broucek J, Horínek A, Mazura I, Zvárová J	Allele frequency data for 17 short tandem repeats in a Czech population sample.	Forensic Sci Int Genet. 2009 Dec;4(1):e15-7.	

Ghana	Poetsch M, Ergin Z, Bayer K, El-Mostaqim D, Rakotomavo N, Browne EN, Timmann C, Horstmann RD, Schwark T, von Wurmb-Schwark N.	The new Powerplex® ESX17 and ESI17 kits in paternity and maternity analyses involving people from Africa--including allele frequencies for three African populations.	Int J Legal Med. 2011 Jan;125(1):149-54	
Iceland	Andreassen R, Pereira L, Dupuy BM, Mevaag B.	Icelandic population data for the STR loci in the AMPFlSTR SGM Plus system and the PowerPlex Y-system.	Forensic Sci Int Genet. 2010 Jul;4(4):e101-3.	
Iran	Shepard EM, Herrera RJ.	Iranian STR variation at the fringes of biogeographical demarcation.	Forensic Sci Int. 2006 May 10;158(2-3):140-8.	
Nigeria	Hohoff C, Schürenkamp M, Brinkmann B.	Meiosis study in a population sample from Nigeria: allele frequencies and mutation rates of 16 STR loci	International Journal of Legal Medicine, 2009, Volume 123, Number 3, Pages 259-261	
Norwey	Andreassen R, Jakobsen S, Mevaag B.	Norwegian population data for the 10 autosomal STR loci in the AMPFlSTR SGM Plus system.	Forensic Sci Int. 2007 Jul 20;170(1):59-61	
Pakistan	Rakha A, Yu B, Hadi S, Sheng-Bin L.	Population genetic data on 15 autosomal STRs in a Pakistani population sample.	Leg Med (Tokyo). 2009 Nov;11(6):305-7.	
Romania	Barbarii LE, Rolf B, Constantinescu C, Hohoff C, Calistru P, Dermengiu D.	Allele frequencies of 13 short tandem repeat (STR) loci in the Romanian population.	Forensic Sci Int. 2004 May 10;141(2-3):171-4.	

Russians	Stepanov VA, Melnikov AV, Lash-Zavada AY, Kharkov VN, Borinskaya SA, Tyazhelova TV, Zhukova OV, Schneider YV, Shil'nikova IN, Puzyrev VP, Rybakova AA, Yankovsky NK.	Genetic variability of 15 autosomal STR loci in Russian populations.	Leg Med (Tokyo). 2010 Sep;12(5):256-8. Epub 2010 Jul 13	Russians from 5 Russian cities (Belgorod, Orel Yaroslavl, Orenburg, Tomsk)
Rwanda	Tofanelli S, Boschi I, Bertoneri S, Coia V, Taglioli L, Franceschi MG, Destro-Bisol G, Pascali V, Paoli G.	Variation at 16 STR loci in Rwandans (Hutu) and implications on profile frequency estimation in Bantu-speakers.	Int J Legal Med. 2003 Apr;117(2):121-6. Epub 2003 Feb 15.	Rwanda: Hutu
Sweden	Montelius K, Karlsson AO, Holmlund G.	STR data for the AmpFlSTR Identifiler loci from Swedish population in comparison to European, as well as with non-European population.	Forensic Sci Int Genet. 2008 Jun;2(3):e49-52.	
Tanzania	Forward BW, Eastman MW, Nyambo TB, Ballard RE.	AMPFlSTR Identifiler STR allele frequencies in Tanzania, Africa.	J Forensic Sci. 2008 Jan;53(1):245.	Meru of Tanzania
Ukraine	Stepanov V.A. et al.,	Characteristics of Populations of the Russian Federation over the Panel of Fifteen Loci Used for DNA Identification and in Forensic Medical Examination.	Acta Naturae. 2011. Т. 3. № 2 (9). С. 59-71. (in Russian)	Central and East Ukraine

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