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The Problem of Non-Shared Environment in Behavioral Genetics

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This research was supported by the Russian Foundation for Basic Research (Grant 15-04-05579)

**Abstract** The role of non-shared environment (NSE) in the development of psychological traits is usually comparable with that of the genotype. However, no specific factors of NSE with significant impact on such traits have been discovered so far. We propose that the current failures in understanding the origin of NSE are at least partly due to the fact that behavioral genetics has left out one of the key sources of phenotypic variation. This source is the intrinsic stochasticity of molecular processes underlying individual development. At the critical stages of ontogeny, even minor fluctuations in gene expression or gene-product functioning can remarkably affect the phenotype; this role is experimentally proved in multiple model organisms. In the present paper, several mechanisms of molecular stochasticity, which could affect the development of psychological traits, are discussed. We propose to distinguish external NSE (any external differences) and internal NSE (intrinsic molecular stochasticity). Available data indicate that the impact of external NSE is likely to be low, which makes the presumptive role of internal NSE rather decisive. If our assumption is true, the paradigm of behavioral genetics should be revised, and comprehensive analysis of molecular stochasticity during individual development is strongly required.

**Keywords** Behavioral genetics · Psychological traits · Non-shared environment · Molecular stochasticity · Phenotype formation

**Introduction**

Twin studies convincingly demonstrate that the impact of genotype on most psychological traits does not exceed 50% (see Bouchard and McGue 2003; Burt 2009;Davis et al. 2009; Keller et al. 2005; Loehlin 1992; Plomin et al. 2013; Polderman et al. 2015); thus, the major or at least substantial role is believed to be played by the environment. Since the mid-20th century it has been widely accepted that shared environment (SE) including parenting style, education, social environment, etc. is of the primary importance. However, with the growing body of factual evidence, it became clear that children reared in the same family differ from each other in their psychological traits almost in the same way as if they were reared in different families. This phenomenon was thoroughly discussed by Plomin and Daniels (1987), and the authors made a revolutionary assumption that the main source of environmental effects on psychological traits was non-shared environment (NSE). Usually, the impact of NSE is at least twice higher than that of SE; moreover, the latter is sometimes zero. This rule seems to be violated only in some cases like reading and verbal abilities, where the role of NSE is either comparable with that of SE or even lower (Table I); such an effect might be due to the impact of language input on the listed traits.

Although NSE is so important for psychological traits, its specific factors are still unclear. As usual, they are just the results of theoretical speculations with no evidential base. Any empirical data are quite rare. Analysis of monozygotic (MZ) twins reared together revealed several possible factors of NSE. These were birth weight discordance, illnesses and accidents, traumatic neonatal life events, difference in parenting style, academic achievement, peer problems, and some others (Asbury et al. 2003, 2006a, 2006b; Deater-Deckard et al. 2001; Mullineaux et al. 2009; Price 1950, 1978). However, the impacts of the mentioned factors on certain psychological traits are rather modest: the effect sizes are usually less than 3% (Asbury et al. 2003, 2006a; Mullineaux et al. 2009). For twin pairs showing the greatest MZ discordance (marginal 10% of the examined samples), the effect size can reach 12%; but this finding does not change the general regularity.

Moreover, correlation between specific environmental factor (for example, parenting style) and certain psychological trait does not mean that the first is the cause of the second. Theoretically, the differences in parenting style might arise when parents either implicitly or explicitly notice even slight but *objective* psychological differences between MZ twins (the possible origins of such differences are considered below). Thus, the attempts to reduce NSE to specific external factors have not been successful so far.

Current failures in understanding the origin of NSE may be explained in several ways. First, NSE includes measurement errors which fundamentally cannot be reduced to any specific factors. However, for many traits, the impact of NSE is about 50% or even higher (see Table I; Polderman et al. 2015). Measurement errors cannot be so huge; thus, the major portion of NSE should be conditioned by specific factors which are to be revealed. Such factors are undoubtedly multiple since any pair of MZ twins is never reared in exactly identical environments, even prenatally.

Second, the search for specific factors underlying psychological trait formation is problematic not only in case of NSE. Similar severities relate to the impact of genotype. Indeed, in genome-wide association studies, numerous loci involved in certain trait formation are elucidated, but the role of any of them appears to be rather modest and their overall influence is much lower than the impact of genotype estimated by twin analysis (for a review, see Zuk et al. 2012). It has been suggested that so called ‘missing heritability’ might be due to epistatic interactions between different loci (see Falconer and Mackay 1996). By analogy, the problem of ‘missing NSE’ might be theoretically explained by epistatic interactions between different external factors.

Third, behavioral genetics still tends to ignore one of the key sources of phenotypic variation. This source is the stochastic nature of molecular processes involved in gene expression and gene-product functioning. Herein, we will discuss the possible role of molecular stochasticity in psychological trait formation.

**The Sources of Phenotypic Variation**

It has been traditionally believed that the phenotype was determined by the interplay between the genotype and environment. Correspondingly, variation of any trait was subdivided into genotypic variation and environmental variation. This is where classic Galton’s dilemma ‘Nature or Nurture?’ and its multiple derivatives (Galton 1875; McCrae et al. 2000; Plomin 1994; Plomin and Bergeman 1991; Ridley 2003) were enrooted. Meanwhile, the reality is much more complex.

First, during individual development, the phenotype changes consistently. For instance, in butterflies and beetles, larva and pupa dramatically differ from imago (see Chown and Gaston 2009), and in some trematodes, different ontogenetic stages of the same species have been initially considered as distinct taxa (see Galaktionov and Dobrovolskij 2003). This means that the phenotype substantially depends on developmental stages; therefore, along with genotypic and environmental variations, ontogenetic variation should be distinguished as well (Estes and Williams 1984; Hayes et al. 2009).

Second, even organisms possessing the same genotype and reaching the same developmental stage under strictly controlled environmental conditions can remarkably differ in their phenotypes. This phenomenon has been known for almost a century as incomplete penetrance, variable expressivity, and fluctuating asymmetry (see Griffiths et al. 2010). Skeleton development in C57/Black6 mice heterozygous for the *M-twist* gene deletion is a spectacular example (Bourgeois et al. 1998). These mice display multiple skeletal anomalies sharply varying between individuals. In particular, about 60% of such individuals display an extra big toe on either one or both hind limbs, whereas the rest 40% are normal.

This variation is neither genotypic (all organisms are of the same genotype), nor environmental (all organisms were kept in the same environment), nor ontogenetic (all organisms are tested at the same developmental stage). Thus, there should be one another source of phenotypic variation. It is referred to as stochastic (random) molecular events affecting phenotype formation (for a review see Ruvinsky 2016; Smith 2011).

**What Is the Nature of Stochastic Processes?**

Modern genetics treats ambiguously the idea of stochasticity. On the one hand, most geneticists are explicit or implicit determinists: they believe that any event is determined by specific causes, although many of them have not been identified so far. Hence, there are no mere accidents, but combinations of yet unidentified causes (see Von Wright 1974). This assumption has emerged from classical mechanics with its idea of causal relationships, and remains highly appealing. The following statement ‘Chance might only be a label for our current inability to identify the environmental processes by which children growing up in the same family come to be so different’ (Plomin 2011, p. 585) is a remarkable example of the deterministic views.

On the other hand, the vast majority of genetic regularities are statistical. These regularities describe the probability of certain events and various influences affecting this probability, but each event itself is considered unpredictable. For instance, ultraviolet rays increase mutation rates in microorganisms (see Auerbach 1976). This effect can be thoroughly measured, and its dependence on numerous external and internal variables (e.g. radiation dose, temperature, nutrient composition, and microbial strain) can be revealed. But it is essentially impossible to predict whether a certain cell will undergo mutagenesis under irradiation and, if so, which exact gene(s) will be affected. These events are random, i.e. stochastic.

The fact that random events do exist was clearly proved by quantum mechanics (Dirac 1935;Landau and Lifshitz 1965). For example, the famous physicist Nils Bohr half-jokingly suggested the idea of the electron’s ‘free will’, referring to the laws of electron motion (see Goswami 2012). Besides, in accordance with complexity theory, each complex system unavoidably goes through critical periods when it should ‘make a choice’ between several alternative pathways (Bar-Yam 1997; Nicolis and Nicolis 2007). This choice is affected by many external factors, including random events (Neimark and Landa 1992; Schroeder 1991). Thus, even if all the parameters are strictly controlled, each complex system is unpredictable and can only be described in terms of probability. It is still unclear whether this phenomenon is a direct consequence of quantum stochasticity, or it is conditioned by some mechanisms of higher order.

Any organism is a complex system, too. It also undergoes inescapable random events (Molenaar et al. 1993; Olsen and Degn 1985; Waddington 1962), some of which are important for phenotype formation. Indeed, numerous examples of stochastic phenotypic variation were described (Astauroff 1930; Chang et al. 2008; Clerc and Avner 2011; Gärtner 1990; Kitazawa and Fujimoto 2014; Raj et al. 2010; Raj and Oudenaarden 2008; Tvorogova et al. 2017; Wernet et al. 2006). At present, it is impossible to prove rigorously that this variation is brought about by random (quantum) events without any latent causes. Nevertheless, while the nature of these phenomena remains a blind-spot, we should also consider the fourth type of variation, which is based on admittedly random events, in addition to genotypic, environmental, and ontogenetic variations.

The fourth type of variation is called in different ways. It is known as weak expression of a trait (Timofeeff-Ressovsky 1925), incomplete penetrance and variable expressivity (Vogt 1926), random variation (Gärtner 1990), realizational variation (Strunnikov and Vyshinsky 1991), epigenetic somaclonal variation (Kaeppler et al. 2000), fluctuational variation (Tikhodeyev 2013), or stochastic developmental variation (Vogt et al. 2015). In our view, the terms ‘random variation’ and ‘fluctuational variation’ are preferable: each term covers all the corresponding phenomena irrespectively of the details of their manifestation, and directly points to their origin (any stochastic events affecting phenotype formation). Further, we will use the latter one. We believe that the term ‘fluctuational’ is more suitable than ‘random’ since it does not induce an erroneous impression that the phenotype is controlled by random events exclusively. Indeed, each fluctuation is a stochastic deviation from the state that is determined by the genotype, environment, and developmental stage; so, their roles are also taken into account.

**Molecular Basics of Fluctuational Variation**

Any chemical reaction, especially a complex one, is a stochastic process (Frank-Kamenetsky 1967; Zhabotinsky and Zaikin 1973). This relates to (i) the reaction rate, (ii) the catalyst specificity, and (iii) various threshold effects (e.g. minimal required concentrations of the components). As a result, stochastic dispersion of outcomes takes place.

There is a large body of evidence confirming that stochastic events are typical for all molecular genetic processes. In particular, DNA replication is unavoidably followed by random errors even in the absence of any mutagens (Bresler et al. 1973; Drake et al. 1988). Random errors occur during gene expression: they affect the primary structure of the corresponding RNAs and proteins (Cochella and Green 2005; Rosenberger and Hilton 1983; Stansfield et al. 1998). The efficiency of gene expression fluctuates as well (Elowitz et al. 2002; Raj et al. 2006; Raser et al. 2004). Moreover, the same gene can be stochastically expressed in different (alternative) ways; as a result, several different products can be produced (Landry et al. 2003; Ochsenreiter et al. 2008; Sachs et al. 1997; Staiger and Brown 2013; Zeremski et al. 1999).

At the critical stages of individual development, even minor fluctuations in gene expression or gene-product functioning can strongly affect phenotype formation. This is proved experimentally for a wide range of species from bacteria to mammals (see Table II). A good example of fluctuational variation in humans is described below.

At the early stages of female embryo development in all placental mammals and particularly in humans, one of the two *X*-chromosomes is inactivated as a Barr body (Avner and Heard 2001; Briggs et al. 2014). The key events occur at the blastocyst stage, when the embryo consists of numerous (from several to more than hundred) cells. Each of these cells makes a random ‘decision’ which *X*-chromosome (maternal or paternal) will be inactivated, and the ‘decision’ is retained in subsequent cell divisions. As a result, the female becomes mosaic. The phenotypic effects of such mosaicism are well known in human females heterozygous for the *EDA* mutation. This mutation results in ectodermal dysplasia and, in particular, leads to perspiratory gland absence; thus, depending on what *X*-chromosome (with the mutant or wild type allele) is active, some skin areas are defective in sweating, while the others are normal (Sun and Tsao 2008). The considered mosaicism is random. Therefore, even MZ sisters reared in very similar environment will differ in the distribution of their normal and defective skin areas.

**Possible Impact of Fluctuational Variation on Psychological Traits**

The behavior of an organism is a stochastic process. It depends on numerous variables (the genotype, the environment, the developmental stage, prior experience, expected results, etc.) including some random events (Brunswik 1939; Falmagne 1965; Koshland 1984). Therefore, the vast majority of psychological traits are, in fact, statistical indicators. For example, a deceitful person produces not only lies; he/she differs from a truthful one in substantially higher frequency of false statements. Moreover, by tracing the statements of a deceitful person, it is impossible to predict what sort of lie will be told next and when exactly it will happen.

Every human manifests some unpredictability in his/her behavior. This affects choices in certain situations but usually has no impact on the person’s psychological traits (in other words, on statistically replicable parameters of a certain person) and, therefore, is of no particular interest for this paper. However, even under strictly controlled conditions (i.e. in MZ twins reared together) some random events may lead to noticeable long-term psychological discordance. Let us look at some examples of such cases.

During the development of the nervous system, numerous synaptic connections are built. The number and location of these connections are under complex molecular genetic control, but the role of stochastic events is also significant (Braitenberg and Schüz 1998; Feldmeyer and Lübke 2010; Kaiser et al. 2009; Merchán-Pérez et al. 2014). Thus, even two MZ twins reared in completely identical environment should inevitably differ from one another in the number and exact location of their synapses (Changeux and Garey 1997). Although this hypothesis is hard to be tested in humans due to an enormously high amount of neurons in the human nervous system, it was already confirmed for some model organisms. In isogenic crustaceous *Daphnia*, the extent of axon branching for identical neurons is shown to be different (Macagno et al. 1973); in nematode *Caenorhabditis*, certain axon targeting is a result of random molecular events (Kulkarni et al. 2013). It seems likely that similar phenomena should also be common in humans. In its turn, differences in the synapses number and location can affect some behavioral traits (Akay et al. 2006; Burgess et al. 2009; Connell-Crowley et al. 2007; Gallea et al. 2011). Thus, it is quite possible that random events in synapse formation are one of the mechanisms underlying fluctuational variation of psychological traits.

In classical genetics, it was universally accepted that in any heterozygote both alleles are expressed, and the phenotype depends on their interplay. Meanwhile, many exceptions to this rule have recently been described. It has turned out that in different cells of the same organism, different alleles from the pair can be expressed solely, and this ‘choice’ can be random. This phenomenon is referred to as random monoallelic expression. It is common for all placental mammals including humans (Chess 2013; Gimelbrant et al. 2007; Zakharova et al. 2009). Two forms of random monoallelic expression are known.

First, as it was noted above, one of the two *X*-chromosomes is randomly inactivated in different cells during female embryogenesis. The underlying mechanisms include DNA methylation and histone modifications (see Allis et al. 2007), which belong to a wide spectrum of epigenetic processes providing inheritance without any changes in DNA sequences (for a review, see Jablonka and Lamb 2005; Tikhodeyev 2018). As a result, random inactivation of the X-chromosome is stably inherited in cell lineages during individual development, and any structure of a female organism including the nervous system appears to be mosaic. *X*-chromosome carries about 1000 genes (Ross et al. 2005), and about one hundred of them affect neuronal functions. Therefore, if a woman is heterozygous for any of these genes, and the corresponding alleles substantially differ in their manifestation, her brain should be functionally mosaic. This mosaicism is random and unique to every woman. Therefore, even MZ sisters reared in exactly identical environment may differ in their brain mosaicism and eventually display remarkable psychological discordance.

Second, random monoallelic expression also affects a number of autosomal genes. This phenomenon is likely to be similar to *X*-chromosome inactivation; however, it is equally inherent in both sexes and relates to comparatively small genomic regions rather than to entire chromosomes. For each region, the ‘decision’ is usually taken independently. After the ‘choice’ is made in each embryonic cell separately, the results remain in subsequent cell divisions and eventually lead to mosaicism of the organism. This mosaicism is also random and, therefore, differs even in MZ twins. Notably, monoallelic expression involves about 10% of all examined autosomal genes (Gimelbrant et al. 2007) and, thus, may remarkably affect phenotype formation. Moreover, some of the affected genes (e.g. *COMT*, *ROBO1* and *FOXP2*) are responsible for certain psychological traits (Adegbola et al. 2015; Zakharova et al. 2009). It should be also noted that certain epigenetic markers are important for speciation of neuronal subtypes (Kozlenkov et al. 2016; Luo et al. 2017; Mo et al. 2015) and for numerous brain functions (see Bonnaud et al. 2016; Grigorenko et al. 2016; Kim and Kaang 2017; Phan and Bieszczad 2016). Thus, stochastic differences in epigenetic marking are another possible source of psychological discordance conditioned by fluctuational variation.

Third, during the development of a multicellular organism, some somatic mutations occur inevitably. In the absence of any mutagens, their rate is usually low: 10-2 – 10-6 per cell division per genome (Araten et al. 2013; Lynch 2010). However, since an adult human organism possesses several trillion cells, the amount of those carrying somatic mutations runs to billions (Sverdlov and Mineev 2013). Most of them remain functionally and structurally normal (the majority of mutations emerge in ‘junk’ genomic regions and, therefore, have no or very modest impact on the phenotype). But if a mutation affects some functional genomic region, this might notably impact on the features of the mutant cells. The effect is even more perceptible if a mutation emerges at the early stages of embryogenesis; in this case, all the descendants of the initial mutant cell will also be mutant. As a result, the adult organism will possess a large mutant ‘section’ with certain functional or structural defects.

Somatic brain mutations are also inevitable. The human brain consists of several hundred billion neurons, among which many millions must be mutant. What neurons are affected by somatic mutagenesis, and what genes in a certain neuron are mutated, is a matter of random errors in DNA replication. Thus, even MZ twins reared in strictly the same environment should differ from one another in the spectrum and distribution of somatic mutations in their brains (De 2011). This is also a possible source of psychological discordance.

Thus, there are at least three possible mechanisms underlying fluctuational variation of psychological traits; they include the stochastic nature of axon branching and synapse formation, random monoallelic expression, and somatic mutations. Now, we have an appropriate basis for rethinking the concept of NSE.

**The Origins of NSE**

Just recently, it seemed to be an axiom that any differences between MZ twins are the results of some external influences. Therefore, all the previous attempts to disclose the sources of such differences were externally oriented. Now, it has become clear that molecular stochasticity plays an important role as a mechanism underlying variation of psychological traits (Clerc and Avner 2011; Gärtner 1990;Raj et al. 2010). Even organisms that are strictly identical in their genotypes, environments, and developmental stages display random differences due to molecular stochasticity. Based on these findings, a fundamental biological prohibition has recently been formulated: it is essentially impossible to obtain fully identical complex multicellular organisms, particularly in humans (Sverdlov 2009).

Thus, the term ‘NSE’ covers two distinct phenomena. One of them, an *external non-shared environment* (ENSE), is a complex of all external influences affecting a given organism. The second one, an *internal non-shared environment* (INSE), refers to all molecular stochasticity that occurs during individual development (here and below we assume that measurement errors in adequate studies are minimal). Up to now, in all studies that were aimed to disclose specific NSE factors, only the first phenomenon was examined (Asbury et al. 2003, 2006a, 2006b; Deater-Deckard et al. 2001; Mullineaux et al. 2009). This strategy has been hardly successful so far. In our view, this is an indirect evidence that the main source of NSE is not ‘outside’ of the organism, and psychological differences between MZ twins are mostly conditioned by internal factors. In other words, psychological traits are affected by stochastic molecular events to a greater extent than by external influences.

The proposed suggestion is far from being proved yet. However, it is in good agreement with several unique studies (not in humans), where the roles of stochastic events and external influences were thoroughly compared. In particular, during long-term studies in rats, it was shown that the weight of isogenic animals was significantly more affected by random events than by any external influences (Gärtner 1990). Similar suggestion concerning various traits was obtained in silk moth (Strunnikov and Vyshinskiy 1991).

The basic idea that NSE is probably conditioned by some random events (‘choice’) has already been suggested in some behavioral genetic papers (Turkheimer and Waldron 2000; Plomin 2004, 2011; Plomin et al. 2001). Moreover, the potential role of random events at the level of DNA methylation has also been proposed (Plomin 2011). However, these papers treated any random differences as the result of some unknown external causes; so, they approached the problem from a strictly deterministic perspective, which led to the fact that the role of the inward stochasticity was not accounted.

The possible impact of internal stochasticity on individual development has been also proposed by numerous authors (Gärtner 1990; Molenaar et al. 1993; Smith 2011; Strunnikov and Vyshinskiy 1991; Vogt 2015; Waddington 1962; Wright 1920). This idea is quite close to ours, but the listed authors considered internal stochasticity as the *third* source of phenotypic variation beyond genotypic and environmental differences; the same point of view remains either explicitly or implicitly even in recent papers describing the mechanisms of molecular stochasticity (see Raj and Van Oudenaarden 2008; Smith 2011). Meanwhile, there are four, not three, sources of phenotypic variation: genotypic differences, environmental influences, ontogenetic stages, and internal molecular stochasticity (see Tikhodeyev 2013; 2016). Thus, our concept of NSE is a further step in the development of theoretical frameworks of behavioral genetics and phenotype formation in general.

**Conclusions**

We have asserted that the term ‘NSE’ comprises two different phenomena. One of them refers to the external influences affecting a given organism, and the other implies internal molecular stochasticity taking place during individual development. Thus, to avoid terminological confusion, it is necessary to distinguish ENSE and INSE, respectively.

So far, the known factors of ENSE are rather few, and their role in the development of psychological traits seems to be low (Asbury et al. 2003, 2006a; Mullineaux et al. 2009). These data might be explained in two ways. First, the impact of ENSE might be, indeed, negligible. Second, the role of ENSE might be substantial but either the majority of the corresponding factors are still unidentified, or there are epistatic interactions between them. To understand which explanation is correct further extensive studies are required. Several branches of such studies could be suggested.

The first branch includes answering the question whether the already known NSE factors are external or internal: at least some of them might be conditioned by INSE. For example, the differences in parenting style might reflect fluctuational variation of some psychological traits in MZ twins. Even in the case of accidents and illnesses, their real origin might be fluctuational variation in attention, novelty seeking, cleanliness, health, etc. For instance, if one member of a MZ pair possesses a higher level of novelty seeking than the other, it might get him/her in a higher number of accidents. To verify the origin of a certain NSE factor, specific empiric approaches will be required such as longitude monitoring of MZ twins and their environment, starting from the very early postnatal stages. Moreover, to minimize measurement errors, only comprehensive direct observations will be appropriate, not questionnaires which often lead to biased reports. It should be noted that different twin pairs may vary in the origin of the same NSE factor.

The second branch implies the search for still unidentified ENSE factors and their effects on the development of psychological traits. Even in inbred mice treated under rigorously equated protocols, the existence of cryptic external factors that are specific to a certain lab and systemically affect animal behavior is shown (Crabbe et al. 1999). It is reasonable to propose that some ENSE factors, affecting psychological trait formation in humans, also remain unknown. Disclosure of such factors and measuring their effects will allow to estimate the overall additive impact of ENSE.

The third branch suggests elaboration of empiric approaches for unraveling epistatic interactions between different ENSE factors. If successful, these studies will demonstrate what portion of ‘missing NSE’ is conditioned by ENSE; the rest should be the impact of INSE.

To carry out the abovementioned studies in humans is a very difficult task. Therefore, it seems useful to start with model genetic organisms like nematodes, drosophila, mice, and rats. The fact is that the term NSE is valid for any trait in any living organism (Polderman et al. 2015; Smith 2011), and the same concerns the impact of molecular stochasticity (Smith, 2011). Indeed, even in isogenic organisms reaching the same developmental stage under identical environment, dramatic fluctuational variation of morphological, physiological, and behavioral traits can be obtained (Bourgeois et al. 1998; Gärtner 1990; Strunnikov and Vyshinskiy 1991; Vogt et al. 2015). In some cases, the stochastic origin of such variation has already been proved, and the underlying mechanisms have been elucidated (Chang et al. 2008; Gordon et al. 2009; Raj and Van Oudenaarden 2008; Sun and Tsao 2008; Tchuraev et al. 2006; Wernet et al. 2006). In the 20th century, the traits displaying remarkable fluctuational variation were usually rejected from genetic analysis as ‘inconvenient’. Now, these become of special interest as a tool to study the effects of molecular stochasticity. Comprehensive analysis of the mechanisms producing fluctuational variation of behavioral traits in model genetic organisms will be a significant step towards unveiling the role of INSE in the development of human psychological traits.

If this role is substantial, the major source of psychological differences between children reared in the same family appears to be internal. It includes distinct genotypes (in case of siblings and dizygotic (DZ) twins), distinct ontogenetic stages (in case of siblings), and molecular stochasticity (in case of siblings, DZ twins, and MZ twins). If so, the impact of nurture on the development of psychological traits is greatly overestimated and approval of traditional behavioral genetic concepts is required.

Notably, the role of INSE is not to be perceptible for any given trait; for some traits, including most important, specific canalizing systems may occur (Waddington 1962). MZ correlations in human skeletal domain are very high (0.83; Polderman et al., 2015); herein, the overall impact of NSE is just 17%, and the effect of INSE might be modest. However, for the traits where MZ correlation is lower, the role of INSE may be really substantial.

**Acknowledgements**

The authors are grateful to anonymous reviewers for their very helpful commentaries and to Maria Lebedeva for her kind assistance in preparation of the text.

**Funding**

This study was funded by Russian Foundation for Basic Research (Grant 15-04-05579).

**Compliance with Ethical Standards**

Conflict of interest statement:On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

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Table I. The impacts of genotype (A), non-shared environment (ENS) and shared environment (ES) on psychological traits

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Psychological trait  | Na  | A  | ENS  | ES  | Reference  |
| Extraversion  | 12 777  | 0.38  | 0.49  | 0.10  | Loehlin 1992 |
| 12 913  | 0.47  | 0.53  | 0.00  | Keller et al. 2005 |
| Neuroticism  | 12 777  | 0.35  | 0.50  | 0.15  | Loehlin 1992 |
| 18 400  | 0.48b  | 0.52b | 0.00b  | Bouchard and McGue 2003 |
| 0.42c  | 0.58c | 0.00c |
| Impulsivity  | 12 777  | 0.38  | 0.55  | 0.07  | Loehlin 1992 |
| Novelty seeking  | 12 777  | 0.45  | 0.49  | 0.06  | Loehlin 1992 |
| 12 913  | 0.40  | 0.60  | 0.00  | Keller et al. 2005 |
| Altruism | 12 777  | 0.35  | 0.54  | 0.11  | Loehlin 1992 |
| Depression  | 42 054  | 0.44  | 0.42  | 0.14  | Burt 2009 |
| Harm avoidance  | 12 913  | 0.44  | 0.56  | 0.00  | Keller et al. 2005 |
| Antisocial behavior  | 68 244  | 0.75  | 0.25  | 0.00  | Rhee and Waldman 2002 |
| Anxiety  | 41 572  | 0.48  | 0.40  | 0.12  | Burt 2009 |
| Lie  | 12 913  | 0.27b  | 0.69b  | 0.04b  | Keller et al. 2005 |
| 0.34c | 0.57c | 0.09c  |
| Broad externalizing difficulties  | 21 914  | 0.59  | 0.26  | 0.15  | Burt 2009 |
| Broad internalizing difficulties  | 26 198  | 0.51  | 0.33  | 0.16  | Burt 2009 |
| Hyperactivity and attention deficit  | 51 424  | 0.70  | 0.30  | 0.00  | Burt 2009 |
| Conduct problems  | 13 120  | 0.50  | 0.39  | 0.11  | Rhee and Waldman 2002 |
| 57 418  | 0.58  | 0.28  | 0.14  | Burt 2009 |
| Perception speed and accuracy  | 21 788  | 0.64  | 0.36  | 0.00  | Bouchard and McGue 2003 |
| Spatial abilities  | 21 788  | 0.60  | 0.40  | 0.00  | Bouchard and McGue 2003 |
| Memory  | 21 788  | 0.48  | 0.52  | 0.00  | Bouchard and McGue 2003 |
| Intelligence  | 50 470  | 0.48  | 0.35  | 0.17  | Devlin et al. 1997 |
| ~ 10 000  | 0.57  | 0.14  | 0.29  | Davis et al. 2009 |
| 13 306 | 0.58 | 0.38 | 0.04 | Khrapol et al. 2014 |
| Educational abilitiesd | 13 306 | 0.62 | 0.12 | 0.36 | Khrapol et al. 2014 |
| Mathematic abilities  | ~ 10 000  | 0.70  | 0.22  | 0.08  | Davis et al. 2009 |
| Verbal abilities  | 21 788  | 0.48  | 0.31  | 0.21  | Bouchard and McGue 2003 |
| ~ 10 000  | 0.52  | 0.13  | 0.35  | Davis et al. 2009 |
| Reading | ~ 10 000  | 0.70  | 0.13  | 0.17  | Davis et al. 2009 |
| Cognitive domain | ~ 900 000 | 0.47 | 0.35 | 0.18 | Polderman et al. 2015 |
| Neurological domain | ~ 125 000 | 0.50 | 0.43 | 0.07 | Polderman et al. 2015 |
| Psychiatric domain | ~ 4 000 000 | 0.46 | 0.38 | 0.16 | Polderman et al. 2015 |

a only studies with N about 10 000 or more are included

b males

c females

d General Certificate of Secondary Education (English, mathematics, science) at age 16

Table II. The role of molecular stochasticity in phenotype formation

|  |  |  |  |
| --- | --- | --- | --- |
| Object | Process | Mechanism | Reference |
| *E. coli* | Choice of either ON or OFF state of the wild-type *lac* operon under low level of the inducer | Stochastic illegitimate transcription of the *lac* operon leads to heritable ON state, while the lack of transcription results in OFF state  | Gordon et al. 2009 |
| *Bacillus subtilis* | Choice of either competent or non-competent state for DNA uptake | Stochastic illegitimate transcription of *comK* leads to stable competent state, while the lack of transcription results in non-competent state | Maamar et al. 2007 |
| Yeast | Meiosis under starvation | Stochastic variation in Ime1 protein production provides variation in meiosis timing | Nachman et al. 2007 |
| Nematode | Intestinal speciation in embryos homozygous for some *skn-1* mutant alleles  | Stochastically varying transcription of the genes regulated by the *skn-1* mutant allelesleads to incomplete penetrance of the mutant phenotype  | Raj et al. 2010 |
| Drosophila  | Formation of ‘pale’ and ‘yellow’ ommatidias in eyes  | Stochastic short burst expression of *spineless* in some R7 cells leads to ‘pale’ ommatidia formation, while the lack of this expression results in ‘yellow’ ommatidia | Wernet et al. 2006 |