Gene Environment Interaction–A White Elephant? or An Elephant in the Room?

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Letter to Editor

Genomic information can be considered as “codes” which can’t be altered throughout the lifespan. With the advent of Genome wide association studies (GWAS), the gene-environment interaction is gaining importance in correlating the endophenotypes of psychological abnormalities with genomic variations. The environmental information collected at the time of disease onset can be matched with DNA information to predict vulnerability in disease cohort. Differences between twin heritability studies and single nucleotide polymorphism heritability studies (“heritability gap”) emphasize the key role of “nurture” in the pathophysiology of mental disorders. In addition, Mendel’s second law (law of random assortment) can serve as a useful tool in studies analyzing gene-environment interactions as they help in stratifying patients according to genetic variants.

The variations in pair-bonding, infant attachment and type of responses to negative effect in marital life can also be accountable if we corroborate the pivotal role of genetic polymorphisms with dynamics of relationships. For example, functional variants of the DRD4 (dopamine receptor) gene polymorphism may thus be involved in infant engagement and activity level during interactions with caregivers.

Recent relationship studies tend to measure the “evocative” gene-environment correlations. Individuals react to evocable stimuli based on their inherited characteristics and this determines their ability to sustain in relationships. From a hard-core geneticist point of view, these studies are potentially difficult to elucidate the measure of interaction. Moore and Thoemmes postulated that different plausible configurations of environmental influences can bias the studies done to estimate candidate gene’s interactions with the environment. In developing countries like India, where environmental influences cannot be explicitly modelled, the planning of studies become still more difficult. For example, an Indian researcher is interested in investigating whether a particular genetic polymorphism can influence the quality of close relationships and help in predicting relationship failures such as divorce. Although unrelated to the primary hypotheses, multiple independent variables such as socio-economic status, relationship with first and second degree relatives and cultural aspects can intervene, making the estimates of true gene-environment effects more difficult. This intricacy possibly repels researchers away from this potentially fruitful arena which offers tandem benefits to both a geneticist and a psychiatrist.

Surviving the vulnerability of publication bias, few studies have demonstrated the vantage sensitivity of gene-environment interaction. In a study, nicotinic receptor gene variations were recently found to predict successful abstinence among individuals in smoking cessation trial. In another study, adults with DRD4 7-repeat allele discounted future rewards more steeply if raised in socioeconomically stressed families compared with affluent families. Thus genetic polymorphisms provide a substrate for individual differences in sensitivity to environmental measures.

To summarize, we are in the midst of an evolving paradigm, where the critical individual differences of an individual can be etched out. At its inception, genetics in psychiatry, particularly the gene – environment interaction was seen as a “white elephant” and it remained as a conundrum to researchers. In the era of personalized medicine, ignorance about this entity would
rather be seen as an “elephant in the room”. Clinician-scientists from psychiatry should collaborate with molecular geneticists to understand how specific genes and environments combine to affect behaviour. Sealing the existing Knowledge-translation gap between the disciplines of psychiatry and genetics, is of great aid to budding psychiatrists which helps them to subdivide the patients into genetic subgroups and to offer a personalized treatment.

References


