

The Dhaka University Journal of Linguistics: Vol. 2 No.3 February, 2009
 Page: 173-184, Published on December 2009 by the Registrar, Dhaka
 University ISSN-2075-3098

FOXP2: A gene for language and speech

Hakim Arif ¹

1. Associate Professor, Department of Linguistics, University of Dhaka

Abstract

Establishing the nature of relationship between Linguistics and bio-sciences, especially Genetic Studies is nether an imagination today, nor an ambitious project at all, as psychologists, linguists and genetic scientists started to put there keen interest in this endeavour at the beginning of the twentieth-first century. The study of FOXP2-a potential human gene responsible for the degeneration of half of the members of famous KE family's speech and language performances, starts an epoch-making initiative in this regard. This paper provides a brief description of the research projects dedicated to explore POXP2 gene, including identifying speech and language behaviour of human beings with particular reference to this gene.

Key Words : Grammar gene, language development, autism, SLI, Dyspraxia.

1. Introduction

The interdisciplinary approach to the study of linguistics and other natural sciences turned into a new shape at the beginning of the twenty first century, as molecular scientists put their keen interest in the discipline. Having conducted some insightful research endeavours they identified a special type of human gene called POXP2, which affects the linguistic

The Dhaka University Journal of Linguistics

activities of human beings either partially or at a severe range. In view of the said development in the field, this paper aims at providing with a brief description of the nature and characteristics of such a human gene called POXP2.

Nowadays genomics, a new science dealing with the nature of mapping the genome or protein structure of human body, is a fascinating area of research in biosciences. Scientists in this discipline are frequently getting reflections of the genetic mapping of different physio-neuro-cognitive behaviours as well as manners of human beings hence unfolding the underlying pattern of their polymorphic DNA markers, including amino acid sequence of human proteins and its gene structure (Botstein & Cherry, 1997). Interestingly, the number of such sequences of human gene mapping is exponentially increasing almost every year (Branden & Toose, 1999: 3).

2. Language and human gene

Language, one of the basic neuro-cognitive activities of human beings, has recently been included as a potential area of research in gene studies. Scholars from molecular biology, psychology and linguistics together, hence, are trying to correlate the linguistic performance of human beings with their innate genetic structure. After having observed the nature of deficits and impairments in linguistic activities performed by the KE family pedigree — the famous family-term in recent scientific literature of genomics — they felt interested to conduct research projects on identifying the relation between human gene and language performance. It is worth mentioning that almost forty five years back, linguist Noam Chomsky and neurologist Eric Lenneberg, the two pioneers in the field, first raised the issue of human language ability with their genetic roots (Pinker, 2001: 465).

Vol. 2 No.3 February, 2009

3. Structure of FOXP2

FOXP2 stands for Forkhead bOX 2— the DNA binding domain, a kind of gene mutation identified in pedigree of famous KE family. It severely impairs different language activities of a half of their family members (Marcus and Fisher, 2003: 257). The gene FOXP2 located on human chromosome 7q31 encodes a protein of 715 amino acids belonging to a large family of transcription factors that possess a winged-helix or forkhead box ('fox') (Newbury *et al*, 2002).

According to Kerri Smith (2005), genes of human body are made up of both coding systems and non-coding parts. In genetic studies, coding systems are termed as *exons*, whereas non-coding parts as *introns*. He also informs that the amount and the nature of these exons and introns can vary within the same gene from person to person that leads to a level of complexity of human genome (Smith 2005). With regard to the exonic characteristics of FOXP2, Lai *et al* (2001), the exponents of FOXP2 gene, identify that this gene is organized into 19 exons, and the major splice form encodes a 715-residue protein containing a characteristic of fox domain and a 40-residue polyglutamine tract. Again the polyglutamine repeat is encoded by a mixture of CAG and CAA and has been demonstrated to be stable in normal individuals (Lai *et al*, 2001; Newbury *et al*, 2002).

3.1 FOXP2 of human and other species

FOXP2, responsible for the development of speech and language of human beings, is not a unique gene existing only in human body (Marcus & Fisher, 2003); rather, it has been sequenced in several other species like chimpanzees, gorillas, orang-utans, rhesus, mice and some birds-species with different structure and nature. Enard *et al* (2002) point out that FOXP2 of chimpanzee, gorilla and rhesus macaque identical to each, other but carry only a difference from the mouse and two differences from the human protein, as far as protein structure is concerned. Orang-utans, on the other hand, carry two differences from the mouse and three from humans concerning the number of FOXP2 (Enard *et al*, 2002: 869). In addition, if the polyglutamine tracts are ignored, the human FOXP2

protein differs at only three amino-acids positions with its homologous in mice. The structural variation of human-FOXP2, compared to that of other species, hence can be shown in the figure 1 (Enard *et al*, 2002).

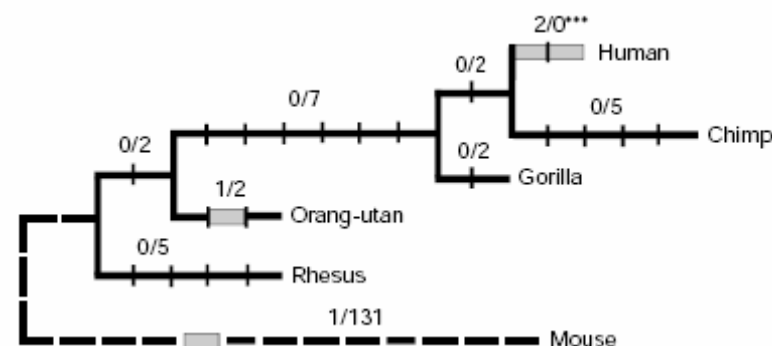


Figure 1 : Structural variation of FOXP2 (source: Enard *et al*, 2002)

3.2 FOXP2 of birds

Some bird species like zebra finch and canary also possess FOXP2 genes that sub-serve their vocal learning process at the different stages. These bird-FOXP2s are to some extent similar to that of human beings in terms of the nature of their expression pattern. But in the striatal nucleus area X, the area necessary for vocal learning for birds, the FOXP2 of zebra finch is expressed at the high level during their vocal learning, whereas in canary it varies seasonally and the expression is observed profoundly when the songs become more unstable (Shu *et al*, 2005).

4. Other biological functions of FOXP2

In the human body FOXP2, a gene is identified not only in the brain area, but also in some other tissues of specific regions responsible for embryo development e.g. lungs, guts and hearts (Marcus, 2003: 261). Lai *et al* (2001) also recognize several members of FOX-class genes in different tissues of the adult organism that tend to create different types of deficits and disorders. For instance, FOXC1 is responsible for congenital glaucoma, FOXE1 for thyroid agenesis, and FOXC2 for lymphedema-distichiasis(LD) syndrome, whereas the deficit

scurfy in the human body is mainly caused by FOXP3, a gene closely related to FOXP2 (Lai *et al*, 2001). In addition, the FOXP2 gene of mice body, which is almost 93.5% similar to its human counterpart, never indicates the ability to their expression as well as language ability. Kerri Smith (2005) highlights that since FOXP2 by nature is highly conserved in evaluation, it is essential for human body not only to develop the brain but also other parts of it (Smith, 2005).

5. FOXP2 as ‘Grammar Gene’

In the contemporary literature of genetic science, especially cognitive genetics FOXP2 is considered a ‘grammar gene’ or ‘language gene’ (Pinker, 1994; Corballis, 2004). It has already been evident that in the pedigree of famous KE family—the famous ‘London family’ suffering from different language and communication problems described in the recent history of genetic studies (Shriberg *et al*, 2006) — the mutated form of this gene creates different types of language disorders for which half of its affected members of first three generations have already been identified as both grammatically and linguistically disabled. The schematic view of the pedigree of KE family is shown in the figure 2. In this figure Watkins *et al*. (2002) provide the signs as – Filled shapes = affected members; open shapes = unaffected members; circle= Females; squares = males; / = deceased.

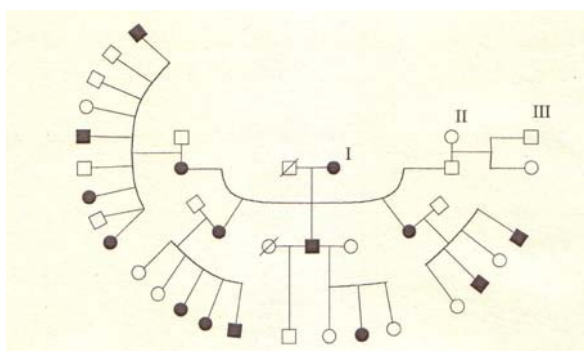


Figure 2 : The Pedigree of KE family (source: Watkins *et al*., 2002)
Such an important finding got enormous attentions, including its detailed structural as well as functional explanations in

many research articles published both before and after 2001, the year identifying FOXP2. Hurst *et al* (1990) first identify the nature of language disorders performed by the members of KE family termed as (severe) *Developmental Verbal Apraxia*. But in some other research experiments conducted in 1990, 1991 and 1997 by Myrna Gopnik and several of her colleagues provide different views in this regard and point out that language problems of KE family are mainly concerned with grammatical deficits rather than exhibiting articulation difficulties mentioned above. More elaborately, they point out that members of the KE family are unable to perform some specific morphosyntactic rules in sentences, especially using features marking of number, gender and tense (Gopnik, 1990; Gopnik and Crago, 1991; Gopnik and Goad, 1997). Considering all previous attempts mentioned, Lai *et al* (2001) — the exponents of FOXP2 gene discovering process — conduct an epoch-making research experiment on the relevant topic of FOXP2 where they diagnose some authentic characteristics of KE family-members’ linguistic disabilities. In their paper, Lai *et al* describe that the affected KE family encounters a serious impairment in selecting and sequencing of fine orofacial movements essential for the articulation of speeches, and that of speech and verbal comprehension. In clinical linguistics, such impairments are as regarded as *Developmental Verbal Dyspraxia* (DVD) or *Orofacial Dyspraxia*, and *Dysphasia* respectively. It is worth mentioning that a very recent study conducted by Vernes *et al* (2008) estimates that 2% of the total population with verbal dyspraxia suffer from mutations in this gene. Below are the descriptions of a wide-ranging aspect of language and grammar that KE family members are unable to perform (Lai *et al*., 2001; Fisher and Marcus, 2006):

1. Language processing-techniques to break up words into their constituent phonemes.

2. Grammatical skills including the production and comprehension of word inflections and syntactic structures. In two different studies, Vargha-Khadem, F. *et al* (1995) and Watkins, K.E *et al* (2002) specify the nature of their deficits, especially in understanding sentences including complex syntactical structures, in distinguishing real words from non-words, reading and in spelling non-words and manipulating phonemes. Thus, *Orofacial Dyspraxia* or inability to coordinate the movement of orofacial tissues for articulation of speech has already been isolated as a core problem of affected KE family, as it causes several other secondary deficits in their language comprehension and production tasks too. At the same time, it also provides a clear demarcation line between the affected and the unaffected members of KE family. In addition to Orofacial Dyspraxia, KE family also encounter some form of *Dysarthria* as well as some type of *Craniofacial Dysmorphology* (Shriberg *et al*, 2006).

Nowadays many scholars desperately link *Orofacial Dyspraxia* of affected KE family to the mutation of FOXP2 gene in their research projects as well as articles on FOXP2. Kerri Smith (2005) mentions that the affected members of KE family carry a single base-pair change in the crucial area of their copies of FOXP2, which causes many problems with the fine mouth movements essentially needed for speeches as well as a hard time understanding of grammar. Enard *et al* (2002), on the other hand, speculate that some human-specific feature of FOXP2 that substitute one or both of the amino-acid in exon 7 affect a person's ability to control orofacial movements. In their study Lai *et al*. (2001) find that affected members carry a heterogeneous missense and a frame shift mutation that change the DNA-binding domain of the FOXP2 protein and hence yields truncated protein products lacking a forkhead domain. The technical detail of this mutation process of FOXP2 gene

described by Lai *et al* (2001) as well as others now is going to be outlined briefly in the following.

6. The nature of the mutation process of FOXP2 and their consequences on language development

FOXP2 protein possesses a stretch of 40 consecutive polyglutamines that follow a second stretch of only 10 glutamines. And this region of FOXP2 is encoded by a mixture of CAG and CAA encodes that have been considered to be highly stable in normal individuals. But in the affected members of KE family such a mutation engage a G→A transition process in exon 14 that co-segregates with/from speech and language disorders in the KE pedigree (Newbury *et al*, 2002). In addition, Lai *et al* (2001) mention-

....We have shown that the FOXP2 gene is directly disrupted by a translocation in a patient with a speech and language disorder, and that a mutation affecting a crucial residue of the forkhead domain of this putative transcription factor co-segregates with a affection status in KE family. We propose that, in both cases, FOXP2 haplo-insufficiency in the brain at the key stage of embryogenesis leads to abnormal development of neural structure that are important for speech and language. [Lai *et al* 2001: 522]

After all, in their article Lai *et al* (2001) emphasize that since haplo-sufficiency of FOXP2 shapes/causes the phenotypes of the affected members of KE family at a crucial stage of embryogenesis, it leads to develop their neural structures concerned with language and speech abnormality.

Another study conducted by Shu *et al* (2005) provides a result ensuring the consistency between the abnormality of cerebellum and the motor deficits observed in the FOXP2. Based on an ultrasonic vocalization study in mice, they observe

that any interference in FOXP2 influences neural migration and/or maturation in the development of cerebellum. And such a disruption in the cerebellar development, finally, underlies the deficits in vocalization of animals affecting its motor activity.

In 2003, Liegeois *et al* conduct a study with a view to determining the pattern of brain activation associated with FOXP2 mutation in the KE family using functional magnetic resonance imaging (fMRI). They isolate some interesting findings on identifying the activation pattern in different brain regions of affected family members in their study. This study shows that mutation in the FOXP2 gene tends to show bilateral abnormality in the functioning of the brain areas responsible for speech and language because underactivation was detected in the right inferior frontal gyrus in a covert verb generation task. The result also finds that under-activations mainly happen in two areas of brains of these affected members i.e. Broca's area and putamen supporting the nature of their morphologically abnormal bilateralism. Underactivation in the Broca's area during the task of repetition of complex non-words by the affected members provides the evidence of *Verbal Dyspraxia*, a core deficit of these members. This result shows that the impairment of speech and language of affected KE family is much less severe than that of aphasic patients which is consistent with the result of previous research project by Watkins *et al* (2002). Finally, the authors conclude that FOXP2 occupies an important role in the development of a putative frontostriatal network involved in the learning and/or planning, and an execution of speech motor sequences similar to that involved in other types of motor skills (Liegeois, 2003).

7. FOXP2 — a potential susceptibility gene for autism and SLI?

Several studies have also been conducted to determine FOXP2 as the potential autism as well as SLI susceptibility gene. Interestingly, no affected member of KE family did exhibit any characteristic of autism or encounter strict diagnostic criteria for SLI. But the overlapping nature between the SPCH1, the locus of human 7q31 where FOXP2 gene is located, and the AUTS1, raised the question of whether a single gene on 7q might be involved in both autism and SLI (Newbury *et al*, 2002; Folstein and Mankoski, 2000). Shu *et al* (2005) mention that most of the research projects on FOXP2 and autism, including '*FOXP2 is not a major susceptibility gene for autism or Specific language impairment*' by Newbury *et al*. (2005) provide a negative result in this respect, though only two studies conducted on Chinese and Japanese on the aforesaid topic observe this association positively. Alongside, the linkage between FOXP2 and SLI has been observed negatively in most of the studies performed. Since FOXP2 gene exhibits heterogeneous genome characteristics, the nature of the mapping process of this gene in relation to language development of human beings has not finished yet. Hence more research projects can be conducted further in this area.

Finally, the recognition of FOXP2 as a potential gene to speech and language activities of human beings is 'offering first the opportunities to the study of language-related neural pathways from a molecular perspective' (Vernes *et al*, 2006; Marcus & Fisher, 2003). Arguably, it opens a new window of making a positive interaction between linguistics and genetics, and creates unlimited scopes to unfold genetic mappings relevant to human language activities as well as their speech and grammatical process. In the near future more scientific research initiatives, I believe, will be carried out in this potential arena.

References

- Branden, C. and Tooze, J. 1999. *Introduction to Protein Structure*. Garland Publication.
- Corballis, M. C. 2004. *FOXP2* and the mirror system. *Trends in Cognitive sciences Vol. 8 No. 3* 95-96
- Botstein, D. and Cherry, J. M. 1997. Molecular linguistics: Extracting information from gene and protein sequences. *Proc. Natl. Acad. Sci.* Vol. 94, pp. 5506-5507
- Enard, W., Przeworski, M., Fisher, S. E., Lai, C. S., Wiebe, V., Kitano, T., Monaco, A. P., and Paabo, S. 2002. Molecular evolution of *FOXP2*, a gene involved in speech and language. *Nature* Vol. 418 869-872
- Fisher, S., and Marcus, G. F. 2006. The eloquent of ape: genes, brains and the evolution of language. *Nature* Vol. 7 9-20
- Folstein, SE, Mankoski, RE. 2000. Chromosome 7q: where autism meets language disorder? *AM J Hum Genet* 67: 278-281
- Gopnik, M. 1990. Feature-blind grammar and dysphasia [letter]. *Nature* 344: 715
- Gopnik, M., & Crago, MB. 1991. Familial aggregation of a developmental language disorder. *Cognition* 39: 1-50
- Gopnik, M., & Goad, H. 1997. What Underlies inflectional error patterns in genetic dysphasia? *J Neuroling* 10: 109-137
- Hurst JA, Baraitser, M., Auger, E., Norell, S. 1990. An extended family with a dominantly inherited speech disorder. *Dev Med Child Neurol* 32: 352-355
- Lai, C. S.L., Fisher, S. E., Hurst, J. A., Vargha-Khadem, F., and Monaco, A. P. 2001. A forkhead-domain gene is mutated in a severe speech and language disorder. *Nature* Vol. 413 519-523
- Liegeois, F., Baldeweg, T., Connelly, A., Gadian, D. G., Mishkin, M., & Vargha-Khadem, F. 2003. Language fMRI abnormalities associated with *FOXP2* gene mutation. *Nature Neuroscience* 6 1230-1237
- Marcus, G. F. and Fisher, S. E. 2003. *FOXP2* in focus: what can genes tell us about speech and language? *TRENDS in Cognitive sciences Vol. 7 No. 6* 257-262
- Newbury, D.F., Bonora, E., Lamb, J.A., Fisher, S.E., Lai, C.S., Baird, G., Jannoun, L., Slonims, V., Stott, C.M., Merricks, M.J., Bolton, P.F. Baily, A.J., Monaco, A.P., and the International Molecular Genetic Study of Autism Consortium. 2002. *AM J Hum Genet* 70: 1318-1327
- Pinker, S. 1994. *The Language Instinct*. Allen Lane
- Pinker, S. 2001. Talk of genetics and vice versa. *Nature* Vol. 413 465-466
- Shu, W., Cho, J. Y., Jiang, Y., Zhang, M., Weisz, D., Elder, G. A., Schmeidler, J., Gasperi, R. De, Sosa, M. A., Gama, R., Donald, S., Anthony C., Perl, D., Morrissey, E., and Buxbaum, J. 2005. Altered ultrasonic vocalization in mice with a disruption in the *Foxp2* gene. *PNAS* Vol. 107 No. 27 9643-9648
- Shriberg, L.D., Ballard, K.J., Tomblin, J.B., Duffy, J.R., Odell, K.H., and Williams, C.A. 2006. Speech, Prosody, and Voice Characteristics of a Mother and Daughter with a 7; 13 Translocation Affecting *FOXP2*. *Journal of Speech, Language and Hearing Research* 49: 500-525
- Smith, K., 2005. *FOX-HUNTING*. *New Scientist* Vol. 188, Issue 2520
- Vargha-Khadem, F. et al. 1995. Praxic and nonverbal cognitive deficits in a large family with a genetically transmitted speech and language disorder. *Proc. Natl. Acad. Sci. U.S.A.* 92, 930-933
- Vernes, S.C., Newbury, D.F., Abrahams, B.S., Winchester, L., Nicod, J., Groszer, M., Alarcon, M., Oliver, P.L., Davies, K.E., Geschwind, D.H., Monaco, A.P., and Fisher, S.E. 2008. A Functional Genetic Link between Distinct Developmental Language Disorders. *The New England Journal of Medicine* 359: 2137-2145
- Vernes, S.C., Nicod, J., Elahi, F.M., Coventry, J.A., Kenny, N., Coupe, N., Bird, L.E., Davies, K.E., Fisher, S.E. 2006. Functional genetic analysis of mutations implicated in a human speech and language disorder. *Human Molecular Genetics* 15; 21: 3154-3167
- Watkins, K.E. et al. 2002. Behavioural analysis of an inherited speech and language disorder: comparison with acquired aphasia. *Brain* 125, 452-464

Email contact : hakimarif.du@gmail.com

