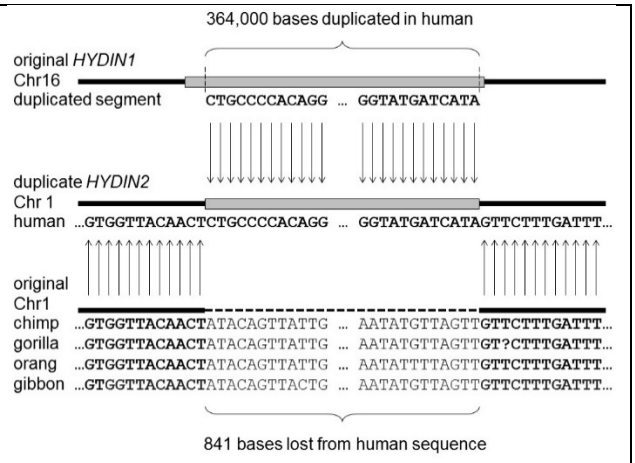
Supplementary material

Comparative genomics are providing pointers to how the human brain has formed over millions of years. Since the time of our last common ancestor with chimpanzees, numerous new genes, including many with putative functions in the brain, have arisen through gene duplication events.[1] An example is the generation of the *HYDIN2* gene (Figure 2). Most of the *HYDIN1* gene on chromosome 16 (364,000 bases) was copied into a site in chromosome 1, generating the daughter gene, *HYDIN2*. The original acceptor site of chromosome 1 is preserved in other apes, and inspection shows that this site lost 841 bases when the *HYDIN* gene sequence was inserted. The new *HYDIN2* gene is active in brain, although its role is not yet known.[2]

Figure 2. A human-specific gene duplication generating *HYDIN2* expressed in brain.

Shown are the original *HYDIN1* gene, located on chr16 (above), the original chr1 sequence (below), and the junction points of the new copied-and-inserted *HYDIN2* gene (centre).

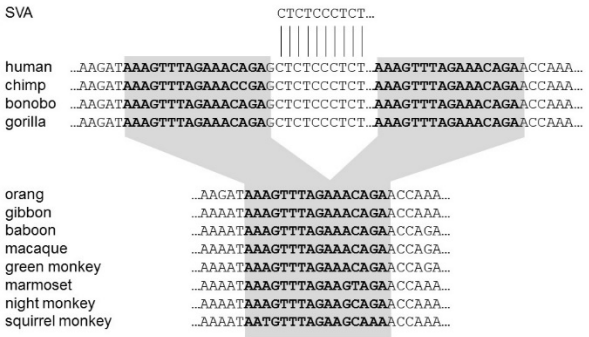
Ref. 63; non-chimp sequences were obtained from the NCBI database by BLAST



It has been hypothesised that gene-regulating networks in brain cells were reconfigured during hominid (great ape) history, and that this rewiring was achieved by the proliferation of hominid-specific 'jumping genes' known as SVA elements. These jumping genes (which are about 1,500 bases long) multiply stochastically by copy-and-paste cycles, during which a DNA original is transcribed into an RNA intermediate, which in turn is reverse-transcribed into a DNA copy at a randomly selected targeted site. The DNA copy is bracketed by duplications of the target site. Some 2,700 are dispersed around the human genome.[3]

SVA elements contain sequence motifs that affect the activities of nearby genes, and many are located near (or in) genes with neural functions. For example, SVA elements, found only in humans, may modulate the activity of the *PARK7* gene[4] and the *FUS* gene[5] (variants of which are associated with neurodegeneration; Figures 3 and 4). Other SVA elements lie near genes encoding neuropeptides[6] and within genes encoding a GABA (neurotransmitter) receptor and a potassium ion channel (Figures 5 and 6).[7] These latter SVA elements are present in humans, chimps and gorillas and thus entered the primate germline in an ancestor of the African great apes.

Future research should clarify whether such SVA elements do in fact possess regulatory activity during brain morphogenesis. What is certain is that their presence establishes human phylogenetic relatedness with other species. For example, humans do share common ancestors with chimps, bonobos, and gorillas (Figures 5 and 6). Any valid theology must take account of this finding.

Figure 3. The insertion site of a human-specific SVA element that may regulate the *PARK7* gene (ref. 65). Here and below, target sites and their duplications are in bold type and shaded. Human SVA and flanking sequences were obtained from the UCSC genome browser; other sequences from the NCBI database by BLAST search; SVA sequences from Kwon *et al* (2013) *Genomics and Informatics* **11**, 142	
Figure 4. The insertion site of a human-specific SVA element that may regulate the *FUS* gene (Ref. 66).	
Figure 5. The insertion site of an African great ape-specific SVA element in the *GABBR2* gene, encoding a neurotransmitter (GABA) receptor (Ref. 68).	
Figure 6. The insertion site of an African great ape-specific SVA element in the *KCNJ6* gene, encoding a potassium channel (Ref. 68).	

Genes that are active in brain cells arose also in ancestors of anthropoid (simian) primates. An insertion (of unknown provenance) gave rise to a gene specifying a regulatory microRNA (*MIR320B1*; Figure 7).[8] The insertion of a jumping gene known as a FLAM (an ancient subclass of Alu element, of which over one million copies are present in human genomes) gave birth to a gene specifying a long non-coding RNA (*BC200*; Figure 8). The *BC200* RNA appears to control protein production in dendrites of neurons.[9]

Figure 7. DNA sequences from the *MIR320B1* gene. An insertion event occurred in an ancestor of anthropoid primates (monkeys and apes) giving rise to the gene specifying miR-320b1. The uninterrupted progenitor sequence is shown for two prosimians. Shaded bases indicate flanking sequence.

Ref. 69 (human, marmoset, aye-aye and galago sequences) and NCBI database (BLAST analysis)

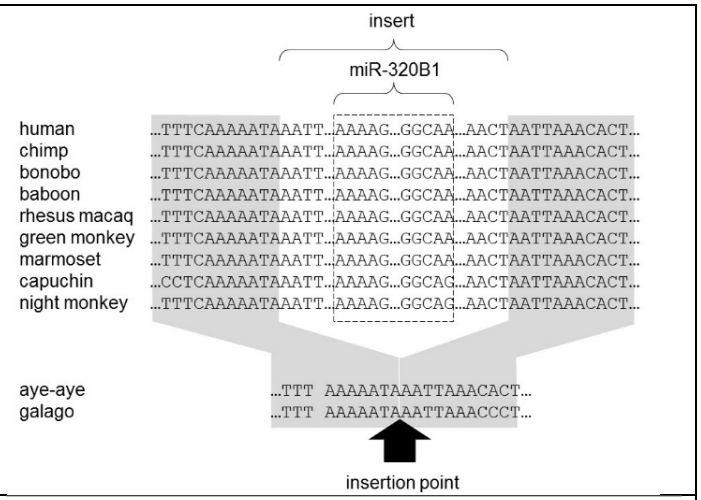
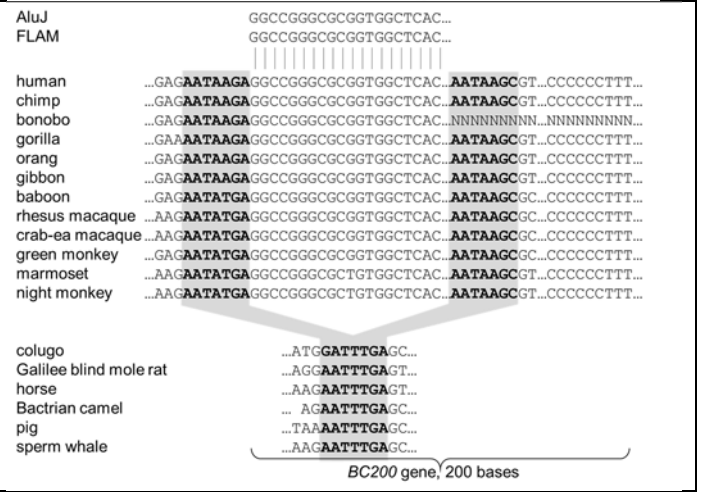


Figure 8. DNA sequences from the *BC200* gene derived from a FLAM element. The insertion event occurred in an ancestor of anthropoid primates (monkeys and apes).
Possible target site and duplications are in bold type and shaded. N, sequence gap. Progenitor sequences cannot be found in prosimians.
Ref. 70 (human, chimp and Alu sequences) and NCBI database (BLAST analysis)



Jumping gene insertions in more remote ancestors have generated putative brain-forming genes. A jumping gene of the 'suchi-ichi' type (studied by Japanese workers) was inserted into the mammalian germline in an ancestor of all eutherian mammals (Figure 9). Sequences belong to this jumping gene were incorporated into a gene, now called *SIRH11*, that is active in brain cells. Surprisingly, the gene has decayed in many lineages. For example, each of seven New World Monkey species carries a gene-disabling two base (GT) insertion, and the unique nature of this insertion establishes the monophylicity of New World Monkeys (Figure 10).[10]

Figure 9. The time when a jumping gene of the sushi-ichi type arose in mammalian evolution. The derived *SIRH11* gene is present in eutherian mammals (but not monotremes or marsupials), but activity has been lost in numerous eutherian clades (as indicated by crosses) (Ref. 71).

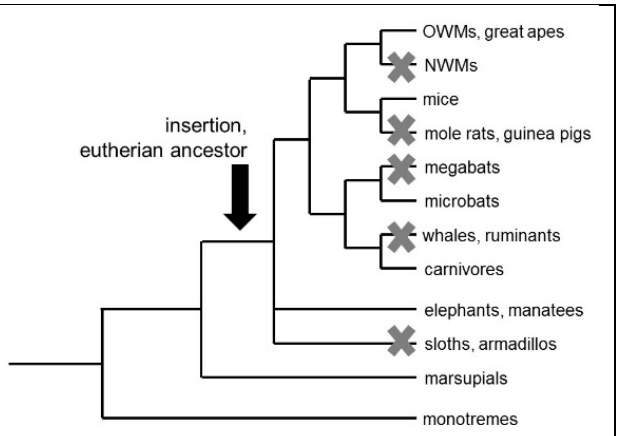
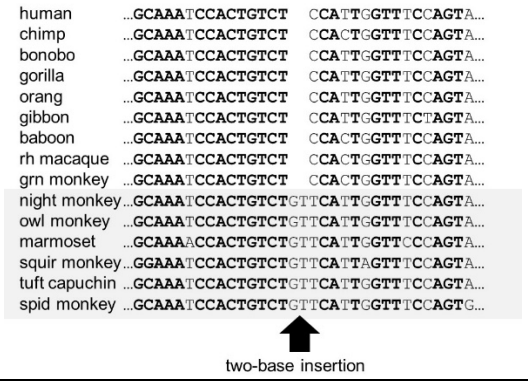


Figure 10. A part of the *SIRH11* gene, showing a mutation (two-base insertion) that occurred in an ancestor of New World Monkeys. No Old World primates possess this insertion. Invariant bases are shown with bold type to indicate conservation of this sequence.

Ref. 71 and additional sequences from the NCBI database.



Jumping genes have contributed to innovations to the pattern of brain development that occurred at the dawn of the mammals. AmnSINE1 elements proliferated in genomes early in mammalian history, and now exist as degenerated relics, apart from particular sequences that have assumed roles in gene regulation. As depicted in Figure 11, many AmnSINE1 elements are shared by all mammals (101 instances, each of which entered the germ-line in a cell ancestral to all extant mammals), by marsupials and eutherians (195 instances), and by eutherians (311 instances).[11] Sequences derived from at least some of these now orchestrate development of the mammalian brain. Sequences from an AmnSINE1 element are present in an ultra-conserved enhancer element that drives brain development in mammals – from platypuses to humans – by turning on the *FGF8* gene (Figure 12).[12] Sequences from another such element – present in marsupials and placental mammals – contribute to a similar outcome by controlling the *SATB2* gene (Figure 13).[13]

Figure 11. Accumulation of AmnSINE1 insertions in amniote genomes (Ref. 72).

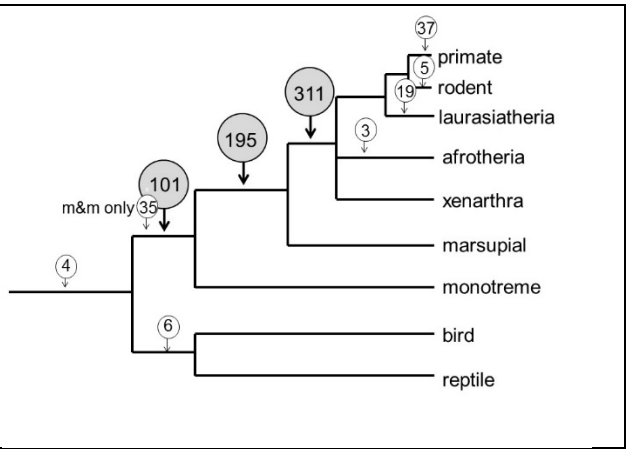
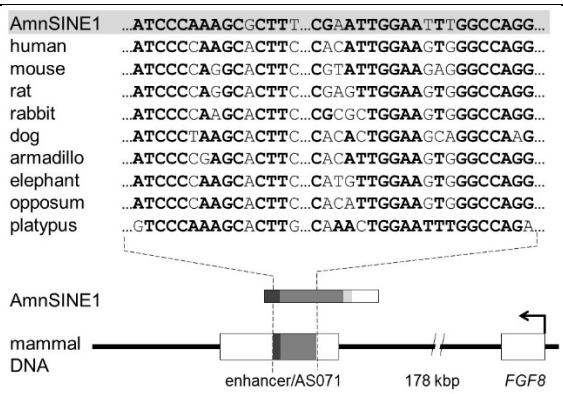
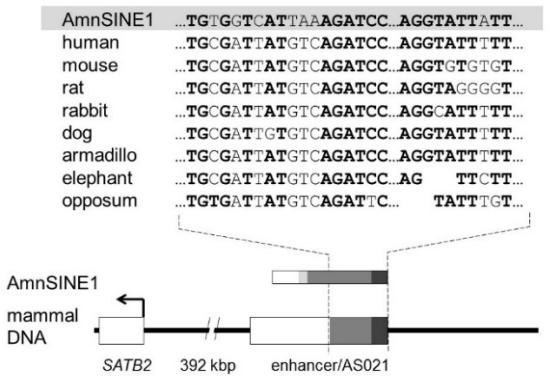


Figure 12. DNA sequences derived from an AmnSINE1 element that activate the *FGF8* gene during brain development (Ref. 73).	
Figure 13. DNA sequences derived from an AmnSINE1 element that activate the *SATB* gene ('special AT-rich sequence binding protein-2', involved in transcriptional regulation and chromatin remodelling) during brain development (Ref. 74).	

These examples provide compelling evidence of human descent from ancestors shared by all humans, with other primate species and, in one case (Figure 12), with all other mammals. They illustrate how myriad tiny incremental steps provided the genetic specifications underlying the unimaginable complexity of the human brain. They emphasise our embeddedness in the materiality of biological history – although that materiality is transformed, transcended and given lasting meaning by relationship with personal agents. It is the thesis of this paper that genes underlying sociality are regulated by by environmental inputs that emanate from communicating, caring and moral beings.