



# Social Neuroscience and Social Genomics: The Emergence of Multi-Level Integrative Analyses

## Neurociencia Social y Genómica Social: El Surgimiento del Análisis Interdisciplinario Multinivel



Editorial

John T. Cacioppo<sup>a,\*</sup> , Stephanie Cacioppo<sup>b</sup> , Steven W. Cole<sup>c</sup> 

<sup>a</sup> Center for Cognitive and Social Neuroscience, University of Chicago, 5848 S. University Avenue, Chicago, IL 60637, United States.

<sup>b</sup> High Performance Electrical Neuroimaging Laboratory, Center for Cognitive and Social Neuroscience, University of Chicago, Chicago, United States

<sup>c</sup> Department of Medicine, Division of Hematology–Oncology, UCLA School of Medicine, Los Angeles, California, United States.

### ARTICLE INFO

#### ABSTRACT

Social neuroscience emerged more than 20 years ago and has grown into a mature interdisciplinary scientific field. Research now provides compelling evidence that the structure and function of the nervous system are influenced by the social environment. Recent work in social genomics further underscores the importance of the social environment by demonstrating the influence of the social environment on gene expression. The multi-level, interdisciplinary approach and the integration of animal models and human research in social neuroscience have proven synergistic and promise continued advances in the delineation of the social brain across species and generations.

#### RESUMEN

La neurociencia social emergió hace más de 20 años y se ha ido convirtiendo en un campo científico interdisciplinario maduro. Ahora las investigaciones proveen evidencia convincente de que la estructura y función del sistema nervioso está influenciadas por el entorno social. Trabajo reciente en genómica social enfatiza más a fondo la importancia del entorno social al demostrar la influencia de este en la expresión génica. El enfoque interdisciplinario multinivel y la integración de modelos animales e investigación humana en neurociencia social han probado sinergia y prometen avances constantes en la delineación del cerebro social a lo largo de las generaciones y especies.

#### Article history:

Received: 09-04-2013

Revised: 13-05-2013

Accepted: 20-05-2013

#### Key Words:

Social neuroscience, social isolation, loneliness, social genomics

#### Palabras Clave:

Neurociencia social, aislamiento social, soledad, genómica social

\* **Corresponding author.** John T. Cacioppo, Center for Cognitive and Social Neuroscience, University of Chicago, 5848 S. University Avenue, Chicago, IL 60637. [Cacioppo@uchicago.edu](mailto:Cacioppo@uchicago.edu) (773.702.1962)



From colonies, swarms, flocks, pods, herds, schools, and huddles, social species by definition form structures that extend beyond the individual. These superorganismal structures evolved hand in hand with behavioral, neural, hormonal, cellular, and genetic mechanisms because of their importance in helping individual members to survive and reproduce. As social neuroscience has matured, it has become evident that the nervous system cannot be considered as an isolated entity i.e., without consideration of the influence of the social environment in which many species live (McEwen & Akil, 2011). Social factors were, nevertheless, once thought to have little relevance to basic biological structure or function, or if they did have relevance they were thought to be too complex to warrant study. When social neuroscience was first proposed, attention had to be given to address why the notion of a social neuroscience was not an oxymoron and why multi-level analyses might contribute to the articulation of comprehensive theories of the structure and function of the brain and behavior (Cacioppo & Berntson, 1992). This was prior to the recognition of the importance of gene regulation and epigenetics in behavior, prior to the discovery of mirror neuron system, and prior to the probes of the human brain in normal waking individuals that exist today (Pearson, 2003). Indeed, genes were still thought to be strong if not invariant determinants of human illness, phenotypes and behavior (cf. Chakravarti & Little, 2003). In less than a decade, new techniques have been developed, that allow scientists to measure how the environment and social factors regulate gene expression and the molecular processes underlying epigenetics, leading to a burgeoning interest in social genomics (Cole, 2009; Slavich & Cole, 2013).

How things have changed. Important advances have been recently made, for instance, in i) neuroscience showing how gene regulation changes complex cognitive functions, including learning and memory, and then causes several developmental and psychiatric disorders effecting language and social functioning (Kendler, Jaffee, & Romer, 2011; Reichenberg, Mill, & MacCabe, 2009); ii) in chromatin biology showing a role for epigenetic mechanisms in long-term memory formation (e.g., Lubin, 2011; Puckett & Lubin, 2011), and iii) in the stress literature with the identification of the effects of early social stress on gene regulation and the epigenome, which then leads to long-lasting changes in behavior, cognition, mood and neuroendocrine responses predisposing to or sheltering from stress-related diseases later in life (e.g., Cole et al., 2012).

There are two alleles for the serotonin transporter gene, short (S) and long (L). Children

with two short alleles (SS) are more likely than children with either a combination of alleles (SL) or two long alleles (LL) to react negatively to the experience of being bullied (Sugden et al., 2010). These genotypes are not equally distributed worldwide, however. Almost half of the population in the United States, Australia, and Great Britain has the S allele, whereas more than three quarters of the population in China (about 80%) has the S allele. These cultures also differ in their emphasis on individualism versus collectivism. Although a number of cultures with lower frequencies of the S allele have more collectivistic cultures than the United States, there is a positive correlation between the percentage of S allele carriers and a culture's rating on a scale from individualistic to collectivistic (Chiao & Blizinsky, 2010). Although multiple relationships are possible, Chiao and Blizinsky (2010) argued that a population with a certain genetic mix might be more likely to form a particular type of culture, a culture might shape the reproductive success of its members, some outside variable could influence both the genetic mix and form of the culture, or some combination of these factors could influence each other simultaneously. People carrying the S allele are especially attentive to negative information (Beevers, Gibb, McGeary, & Miller, 2007; Osinsky et al., 2008). This focus on negativity might assist a person to cope well within a collectivistic environment, as it could lead the early recognition of impending negative interactions might give people a chance to smooth things over before they escalate. The L allele, on the other hand, is associated with more attention to positive stimuli, greater risk-taking, and creativity (Fredrickson, 2001; Isen, Daubman, & Nowicki, 1987), which may be better suited to the individualistic cultural environment.

The social brain hypothesis further suggests that the social environment shaped the very structure and function of the human brain. For instance, Dunbar recently reviewed evidence for the size and connectivity in the primate neocortex as being attributable to the complexity of the social rather than physical environment in which primates evolved (Dunbar, 2009; Dunbar, 2012). Social animals deprived of their natural connections with conspecifics show deleterious effects on cognition, behavior, neural, autonomic, hormonal, and immune function – and similar impairments are observed in humans when they simply perceive they are socially isolated (e.g., Cacioppo & Hawkey, 2009; Cacioppo, Hawkey, Norman, & Berntson, 2011).

Moreover, important advances have also been made in specifying the neural mechanisms underlying a host of social processes, including face perception (Mende-Siedlecki, Said, & Todorov,

2013), mentalizing and theory of mind (Baron-Cohen, 2007; Frith & Frith, 2001), imitation and empathy (Caspers, Zilles, Laird, & Eickhoff, 2010; Decety, Norman, Berntson, & Cacioppo, 2012; McCall & Singer, 2012), cooperation and moral decision making (Moll et al., 2006; Rilling et al., 2002), and love and desire (e.g., Cacioppo, Bianchi-Demicheli, Frum, Pfaus, & Lewis, 2012; Cacioppo & Cacioppo, 2012; Ortigue, Bianchi-Demicheli, Patel, Frum, & Lewis, 2010). This line of research has led to the recognition that social cognition is not supported by a single underlying neural network, but rather social cognition is associated with a variety of networks, each with specific functions including social recognition, social affiliation, and social threat/aversion have been identified (e.g., Bickart, Hollenbeck, Barrett, & Dickerson, 2012). The neural and hormonal substrates for pair bonding are now better understood (e.g., Donaldson & Young, 2008), as are the effects of ostracism and social rejection (Eisenberger & Cole, 2012) and the reciprocal effects of culture and biology (Northoff, 2010; Park & Huang, 2010; Rule, Freeman, & Ambady, 2012).

Many laypeople still think that because something is biological, it is innate and predetermined. Work on the social regulation of gene expression has shown that biological does *not* mean predetermined or invariant. For instance, behavioral and mental processes can influence one's abilities to fight bacteria and viruses (Irwin & Cole, 2011). A person's perception of their social environment influences whether the genes in immune cells are turned on or off to defend against bacteria or viruses (Cole, Hawkey, Arevalo, & Cacioppo, 2011). Human beings formed groups to enhance the odds of their survival. Anyone who was a social outcast was also exposed to a more hostile environment. For instance, finding food, water, and shelter, defending against nonhuman and human threats, dealing with illness and injury, even sleeping without a safe social surround when predators are out at night are more death-defying events for an outcast than for an individual who has others on whom s/he can trust, communicate, and cooperate. Social exclusion not only separated a person from the help of others in life-threatening situations (e.g., fending off predators), but worse yet, it led to outright conflict with others, including combat. Under such hostile circumstances, people who lacked affine connections with others faced a greater risk from bacterial infections than from viruses. This is because bacteria enter the body through cuts and scratches, whereas viruses are transmitted through body fluids (e.g., sneezing). Consequently, people are most likely to be exposed to viruses when they are in close, affine contact with other people. Thus, when individuals feel isolated and left to fend for

themselves, they (like their excluded ancestors) face a greater threat from bacteria than from viruses. In that case, their brains generate signals that tell the genes in the immune system to gear up to protect against bacteria (Eisenberger & Cole, 2012). In contrast, if individuals feel socially connected to others, their brains will initiate a cascade of hormonal signals that tells the genes to prepare to protect against viruses (Cole, Hawkey, Arevalo, & Cacioppo, 2011).

This is just one example of how the brain's representation of the social environment can impact biological processes that are important to cognition, behavior, health and mortality. We could not understand these biological processes or their behavioral relevance if we focused only on the brain (or only on the social situation). Rather, multiple perspectives are necessary to see how the biology of behavior is intimately related to the social context (Cacioppo & Berntson, 1992). The same is true for many of the other psychological (e.g., cognitive, abnormal) perspectives (Cacioppo et al., 2007). To develop comprehensive theories of brain and biological function that have applications to our everyday lives, we may need to consider the role of the social environment.

Social cognition was once described as cognitive psychology applied to social stimuli. It should be apparent that social neuroscience, proposed around the same time as cognitive neuroscience, is *not* simply a cognitive neuroscience approach applied to social stimuli. Social neuroscience represents a complementary perspective in which the brain is viewed, not as a solitary computer, but as mobile information processing device designed for connection at a distance to and interaction with other brains. From the perspective of cognitive neuroscience, language is a system for representation and processing of information; from the perspective of social neuroscience, language is a system for information exchange between brains, a system that promotes connection, communication, and coordination across discrete and sometimes distant brains. Accordingly, the focus in social neuroscience is on a wide range of topics including imitation, social contagion, empathy, attachment, attraction, altruism, aggression, group processes, prejudice, theory of mind, communication, and culture. Social neuroscience, therefore, focuses on specifying the neural, hormonal, cellular, and molecular bases (mechanisms) underlying social processes and behavior. Such an endeavor is challenging because it necessitates the mapping across multiple systems and levels (from molecules to cultures), the efforts of interdisciplinary scientific teams, comparative studies

that bridge the abyss between animal models and human research, multiple innovative methods, and integrative conceptual analysis.

Identifying an association between social and biological factors or processes is only a preliminary step to specifying the mechanism underlying any such association. One of the obstacles to specifying underlying mechanisms is the category error, which refers to the intuitively appealing notion that the organization of cognitive or social phenomena maps in a 1:1 fashion into the organization of the underlying neural substrates. The notion that an engram of a memory or an attitude exists in a localized spot in the brain is an example of what is likely a category error. We anticipate that 1:1 mappings between [brain] and [behavior] will ultimately be achieved. Reaching this ultimate aim, however, may be fostered by the recognition of the preliminary state of our knowledge and the attendant implications for strong inference (Cacioppo, Tassinary, & Berntson, 2000). Given the complementary nature of the data from brain imaging, direct stimulation and lesion studies, and simulation and computational modeling approaches, and molecular and genetic approaches, progress in social neuroscience should be fostered by the integration rather than a progressive segregation of these approaches and literatures.

Perhaps understandably in light of these complexities, contemporary social neuroscience is a broad, interdisciplinary field, with some focused on social insects to understand the genetics of social behavior, others focused on nonhuman animal models to probe the epigenetics and neurobiology of social behavior, others focused on human brain imaging in an attempt to elucidate social cognition, and still others focused on the interplay of social and biological factors underlying human distress associated with atypical social behavior or disease. However, finally, there is also emerging evidence of increased communication among these groups (e.g., Bartal, Decety, & Mason, 2011; Blumstein, 2010; Cacioppo et al., 2007; Decety & Cacioppo, 2011) – an important development for social neuroscience to reach its full potential.

## REFERENCES

- Baron-Cohen, S. (2007). *Theory of mind*. Hove: Psychology Press. Retrieved from [http://www.worldcat.org/title/theory-of-mind/oclc/488257120&referer=brief\\_results](http://www.worldcat.org/title/theory-of-mind/oclc/488257120&referer=brief_results)
- Bartal, I. B. -a., Decety, J., & Mason, P. (2011). Empathy and Pro-Social Behavior in Rats. *Science*, 334(6061), 1427–1430. doi:10.1126/science.1210789
- Beevers, C. G., Gibb, B. E., McGeary, J. E., & Miller, I. W. (2007). Serotonin transporter genetic variation and biased attention for emotional word stimuli among psychiatric inpatients. *Journal of Abnormal Psychology*, 116(1), 208–212. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17324031>
- Bickart, K. C., Hollenbeck, M. C., Barrett, L. F., & Dickerson, B. C. (2012). Intrinsic amygdala-cortical functional connectivity predicts social network size in humans. *The Journal of Neuroscience*, 32(42), 14729–14741. doi:10.1523/JNEUROSCI.1599-12.2012
- Blumstein, D. T. (2010). Towards an integrative understanding of social behavior: new models and new opportunities. *Frontiers in Behavioral Neuroscience*, 4(June), 1–9. doi:10.3389/fnbeh.2010.00034
- Cacioppo, J. T., & Berntson, G. G. (1992). Social psychological contributions to the decade of the brain. Doctrine of multilevel analysis. *American Psychologist*, 47, 1019–1028.
- Cacioppo, J. T., Amaral, D. G., Blanchard, J. J., Cameron, J., Carter, C., Crews, D., ... Quinn, K. J. (2007). Social neuroscience: Progress and implications for mental health. *Perspectives on Psychological Science*, 2(2), 99–123.
- Cacioppo, J. T., & Hawkley, L. C. (2009). Perceived social isolation and cognition. *Trends in Cognitive Sciences*, 13(10), 447–454.
- Cacioppo, J. T., Hawkley, L. C., Norman, G. J., & Berntson, G. G. (2011). Social isolation. *Annals of the New York Academy of Sciences*, 1231, 17–22. doi:10.1111/j.1749-6632.2011.06028.x
- Cacioppo, J. T., Tassinary, L. G., & Berntson, G. G. (2000). *Handbook of Psychophysiology* (2nd ed.). Cambridge: University Press.
- Cacioppo, S., Bianchi-Demicheli, F., Frum, C., Pfaus, J. G., & Lewis, J. W. (2012). The Common Neural Bases Between Sexual Desire and Love: A Multilevel Kernel Density fMRI Analysis. *The Journal of Sexual Medicine*, 9(4), 1048–54. doi:10.1111/j.1743-6109.2012.02651.x
- Cacioppo, S., & Cacioppo, J. T. (2012). Decoding the invisible forces of social connections. *Frontiers in integrative neuroscience*, 6(July), 51. doi:10.3389/fnint.2012.00051
- Caspers, S., Zilles, K., Laird, A. R., & Eickhoff, S. B. (2010). ALE meta-analysis of action observation and imitation in the human brain. *NeuroImage*, 50(3), 1148–67. doi:10.1016/j.neuroimage.2009.12.112
- Chakravarti, A., & Little, P. (2003). Nature, nurture and human disease. *Nature*, 421(6921), 412–

414. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12540911>
- Chiao, J. Y., & Blizinsky, K. D. (2010). Culture-gene coevolution of individualism-collectivism and the serotonin transporter gene. *Proceedings. Biological sciences / The Royal Society*, *277*(1681), 529–37. doi:10.1098/rspb.2009.1650
- Cole, S. W. (2009). Social regulation of human gene expression. *Current Directions in Psychological Science*, *18*(3), 132–137. doi:10.1111/j.1467-8721.2009.01623.x
- Cole, S. W., Hawkey, L. C., Arevalo, J. M. G., & Cacioppo, J. T. (2011). Transcript origin analysis identifies antigen-presenting cells as primary targets of socially regulated gene expression in leukocytes. *Proceedings of the National Academy of Sciences*, *108*(7), 3080–3085.
- Cole, S. W., Conti, G., Arevalo, J. M., Ruggiero, A., Heckman, J. J., & Suomi, S. J. (2012). Transcriptional modulation of the developing immune system by early life social adversity. *Proceedings of the National Academy of Sciences*, *109*(50), 20578–20583. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3528538/>
- Decety, J., & Cacioppo, J. T. (2011). *The Oxford handbook of social neuroscience*. New York: Oxford University Press.
- Decety, J., Norman, G. J., Berntson, G. G., & Cacioppo, J. T. (2012). A Neurobehavioral Evolutionary Perspective on the Mechanisms Underlying Empathy. *Progress in Neurobiology*, *98*(1), 38–48. doi:10.1016/j.pneurobio.2012.05.001
- Donaldson, Z. R., & Young, L. J. (2008). Oxytocin, vasopressin, and the neurogenetics of sociality. *Science (New York, N.Y.)*, *322*(5903), 900–4. doi:10.1126/science.1158668
- Dunbar, R. I. M. (2009). The social brain hypothesis and its implications for social evolution. *Annals of human biology*, *36*(5), 562–572.
- Dunbar, R. I. M. (2012). The social brain meets neuroimaging. *Trends in cognitive sciences*, *16*(2), 101–2. doi:10.1016/j.tics.2011.11.013
- Eisenberger, N. I., & Cole, S. W. (2012). Social neuroscience and health: neurophysiological mechanisms linking social ties with physical health. *Nature neuroscience*, *15*(5). doi:10.1038/nn.3086
- Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *American Psychologist*, *56*(3), 218–226. doi:10.1037/0003-066X.56.3.218
- Frith, U., & Frith, C. (2001). The Biological Basis of Social Interaction. *Current Directions in Psychological Science*, *10*(5), 151–155. doi:10.1111/1467-8721.00137
- Irwin, M. R., & Cole, S. W. (2011). Reciprocal regulation of the neural and innate immune systems. *Nature Reviews Immunology*, *11*(9), 625–632. doi:10.1038/nri3042
- Isen, A. M., Daubman, K. A., & Nowicki, G. P. (1987). Positive affect facilitates creative problem solving. *Journal of Personality and Social Psychology*, *52*(6), 1122–1131. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3598858>
- Kendler, K. S., Jaffee, S. R., & Romer, D. (2011). *The Dynamic Genome and Mental Health*. (K. S. Kendler, S. R. Jaffee, & D. Romer, Eds.) (pp. 195–225). New York, NY: Oxford University Press.
- Lubin, F. D. (2011). Epigenetic gene regulation in the adult mammalian brain: multiple roles in memory formation. *Neurobiology of Learning and Memory*, *96*(1), 68–78. Retrieved from <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3111751&tool=pmcentrez&rendertype=abstract>
- McCall, C., & Singer, T. (2012). The animal and human neuroendocrinology of social cognition, motivation and behavior. *Nature neuroscience*, *15*(5), 681–688. doi:10.1038/nn.3084
- McEwen, B. S., & Akil, H. (2011). Introduction to Social Neuroscience: Gene, Environment, Brain, Body. *Annals of the New York Academy of Sciences*, *1231*, vii–ix.
- Mende-Siedlecki, P., Said, C. P., & Todorov, A. (2013). The social evaluation of faces: A meta-analysis of functional neuroimaging studies. *Social Cognitive and Affective Neuroscience*, *8*(3), 285–299. doi:10.1093/scan/nsr090
- Moll, J., Krueger, F., Zahn, R., Pardini, M., De Oliveira-Souza, R., & Grafman, J. (2006). Human fronto-mesolimbic networks guide decisions about charitable donation. *Proceedings of the National Academy of Sciences of the United States of America*, *103*(42), 15623–15628. doi:10.1073/pnas.0604475103
- Northoff, G. (2010). Humans, brains, and their environment: marriage between neuroscience and anthropology? *Neuron*, *65*(6), 748–51. doi:10.1016/j.neuron.2010.02.024
- Ortigue, S., Bianchi-Demicheli, F., Patel, N., Frum, C., & Lewis, J. W. (2010). Neuroimaging of love: fMRI meta-analysis evidence toward new perspectives in sexual medicine. *The journal of sexual medicine*, *7*(11), 3541–52. doi:10.1111/j.1743-6109.2010.01999.x

- Osinsky, R., Reuter, M., Küpper, Y., Schmitz, A., Kozyra, E., Alexander, N., & Hennig, J. (2008). Variation in the serotonin transporter gene modulates selective attention to threat. *Emotion Washington Dc*, 8(4), 584–588. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/18729589>
- Park, D. C., & Huang, C.-M. (2010). Culture Wires the Brain: A Cognitive Neuroscience Perspective. *Perspectives on Psychological Science*, 5(4), 391–400. doi:10.1177/1745691610374591
- Pearson, H. (2003). DNA: Beyond the double helix. *Nature*, 421(January), 310-312. doi:10.1038/421310a
- Puckett, R. E., & Lubin, F. D. (2011). Epigenetic mechanisms in experience-driven memory formation and behavior. *Epigenomics*, 3(5), 649–64. doi:10.2217/epi.11.86
- Reichenberg, A., Mill, J., & MacCabe, J. H. (2009). Epigenetics, genomic mutations and cognitive function. *Cognitive Neuropsychiatry*, 14(4-5), 377–390. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/19634036>
- Rilling, J., Gutman, D., Zeh, T., Pagnoni, G., Berns, G., & Kilts, C. (2002). A neural basis for social cooperation. *Neuron*, 35(2), 395–405. doi:10.1016/S0896-6273(02)00755-9
- Rule, N. O., Freeman, J. B., & Ambady, N. (2012). Culture in social neuroscience : A review. *Social Neuroscience*, 7(1), 37–41. doi:10.1080/17470919.2012.695293
- Slavich, G. M., & Cole, S. W. (2013). The Emerging Field of Human Social Genomics. *Clinical Psychological Science*. doi:10.1177/2167702613478594
- Sugden, K., Arseneault, L., Harrington, H., Moffitt, T. E., Williams, B., & Caspi, A. (2010). Serotonin transporter gene moderates the development of emotional problems among children following bullying victimization. *Journal of the American Academy of Child & Adolescent Psychiatry*, 49(8), 830–840. Retrieved from <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2908591&tool=pmcentrez&rendertype=abstract>