



# Well connected?

## The biological implications of 'social networking'

One of the most pronounced changes in the daily habits of British citizens is a reduction in the number of minutes per day that they interact with another human being. Recent history has seen people in marked retreat from one another as Britain moves from a culture of greater common experience to a society of more isolated experience. She is in good company, as Americans too step back from one another in unprecedented magnitude.

Aric Sigman

**S**ocial scientists recently reported that in less than two decades “the number of people saying there is no one with whom they discuss important matters nearly tripled”. The number of both kin and non-kin confidants is described as “dramatically smaller” (McPherson *et al*, 2006).

Britons now spend approximately 50 minutes a day interacting socially with other people (ONS, 2003). Couples now

spend less time in one another’s company and more time at work, commuting, or in the same house but in separate rooms using different electronic media devices. Parents spend less time with their children than they did only a decade ago. Britain has the lowest proportion of children in all of Europe who eat with their parents at the table. The proportion of people who work on their own at home continues to rise.

**Title image:** Man at computer. Photo: Geoff Tompkinson/SPL

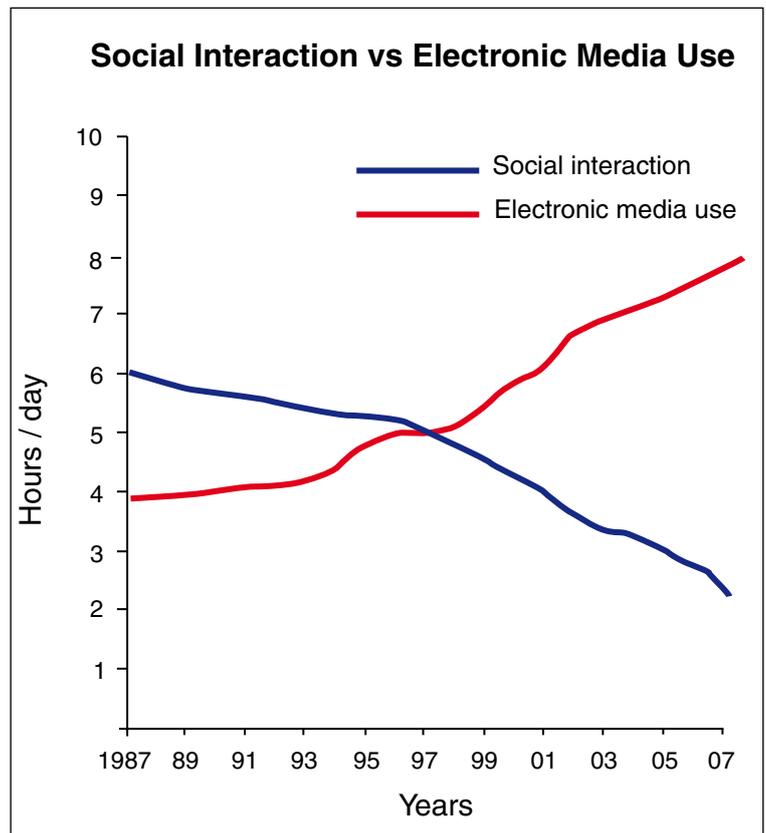
The Office for National Statistics has just reported that “over the last two decades the proportion of people living alone doubled”, a trend now highly pronounced in the 25-44 age group. For the first time in our history a third of the adults in this country live alone, a trend that looks set to continue.

Britain’s disinclination for togetherness is only equalled by her veneration of communicating through new technologies. The rapid proliferation of electronic media is now making private space available in almost every sphere of the individual’s life. Yet this is now the most significant contributing factor to society’s growing physical estrangement. Whether in or out of the home, more people of *all* ages in the UK are physically and socially disengaged from the people around them because they are wearing earphones, talking or texting on a mobile telephone, or using a laptop or Blackberry. An increasing number of deaths caused by the wearers of MP3 players inadvertently stepping into oncoming traffic has led to Senatorial proposals for a New York State ‘distracted walking bill’ to outlaw the use of mobile phones, handheld emailing devices such as Blackberries and video games while crossing a road. Senator Carl Kruger described how people walking around ‘tuned in’ were, in the process of being tuned in, being ‘tuned out’ to the world around them. The malady is referred to as “iPod oblivion”.

### Eye and ear contact

Children now spend more time in the family home alone in front of TV/computer screens than doing anything else (Sigman, 2007). A study by the Children’s Society recently found that television alone is displacing the parental role, eclipsing “by a factor of five or ten the time parents spend actively engaging with children”. Another ongoing study reports that 25% of British five-year olds own a computer or laptop of their own. In particular, the study noted an enormous increase in ‘social networking’ among younger children which “has overtaken fun (online games) as the main reason to use the Internet”. UK social-networking usage is now the highest in Europe. The trend is set to increase: the BBC has recently unveiled the social networking site MyCBBC directed at children as young as six.

Time that was previously spent interacting socially is increasingly being displaced by the virtual variety. A recent editorial of the *Journal of the Royal Society of Medicine* made the timely point that



**Figure 1.** Hours per day of face-to-face social interaction declines as use of electronic media increases. These trends are predicted to increase (data abstracted from a series of time-use and demographic studies).

social networking “...encourages us to ignore the social networks that form in our non-virtual communities. ... the time we spend socialising electronically separates us from our physical networks.” But why precisely should physicians be concerned about these changes in people’s *actual* contact and interaction with one another? Moreover, what does biology have to offer in understanding what appears at first sight to be a demographic phenomenon?

### Genetic alterations

Social connection, both objective and sub-

The developing world is fast adapting to electronic communications as well.

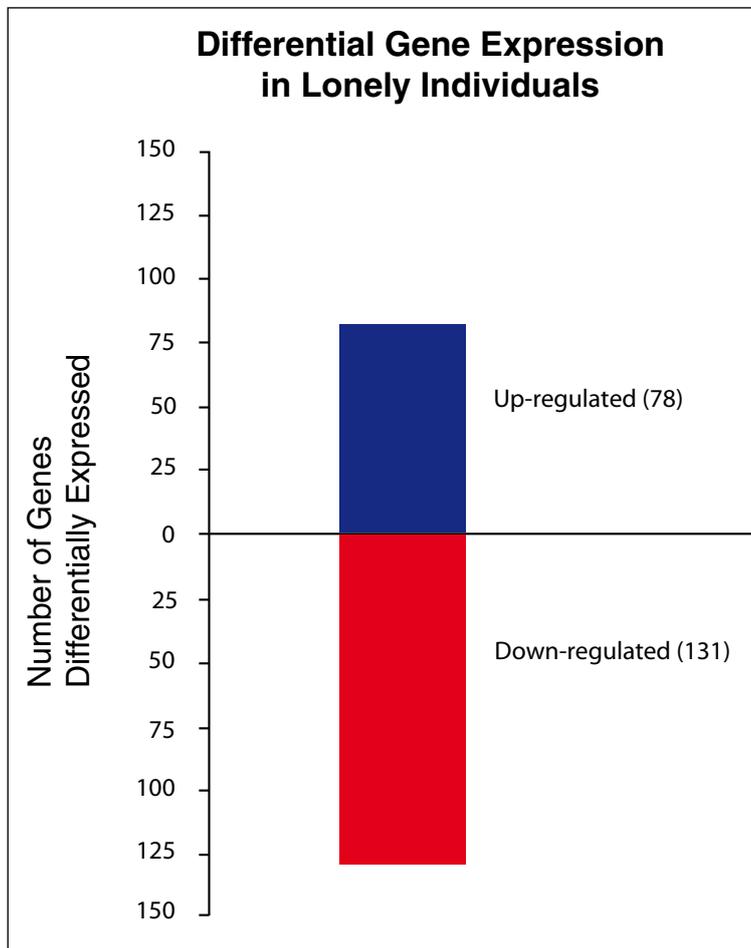




Some parts of the world still do not have access to email and the internet.

jective, is increasingly associated with physiological changes known to influence morbidity and mortality. However, the intricate mechanisms involved are only now being understood. Recent research at the UCLA School of Medicine on the social regulation of gene expression in leuko-

**Figure 2.** A total of 209 genes were differentially expressed in circulating leukocytes of subjects experiencing high subjective social isolation, including up-regulation of genes involved in immune activation, transcription control, and cell proliferation, and down-regulation of genes supporting mature B lymphocyte function and type 1 interferon response. There was a statistically significant net reduction in the number of expressed genes (131 down-regulated vs. 78 up-regulated, difference  $p < 0.0001$  by exact binomial test). (Adapted from Cole *et al.*, 2007.)



cytes, the small white blood cells of the human immune system, has reported the first evidence that social isolation is actually linked to global alterations in human gene transcription in leukocytes. Transcription involves the transfer of genetic information from the DNA molecule to the messenger RNA.

DNA analysis identified 209 genes that were differentially expressed in circulating leukocytes taken from subjects who reported high levels of social isolation versus those reporting low levels. The differences between the groups included the increased expression of genes involved in immune activation, transcription control, and cell proliferation, and the decreased expression of genes supporting the function of the leukocytes (mature B lymphocytes) and Type I interferon response. The researchers found impaired transcription in genes, which is central to our bodies mounting an anti-inflammatory reaction to illness or stress, referred to as a glucocorticoid response. They also observed increased activity in the gene transcription control pathways that *promote* inflammation in disease and stress, and they now believe that this is a functional genomic explanation for the greater risk of inflammatory disease and adverse health outcomes in individuals who experience high levels of subjective social isolation (Cole *et al.*, 2007).

#### Immunological changes

Cytokines are compounds secreted by immune cells that have encountered a pathogen, thereby activating and recruiting further immune cells to increase the system's response to the pathogen. Changes in people's social contact have now been linked to alterations in tumour necrosis factor-alpha (TNF-alpha); an important cytokine associated with tumour regression and increased survival time for cancer patients. In studying the relationship between social contact and TNF-alpha in patients with breast cancer, one team of researchers found that patients reporting increased social activities or satisfaction exhibited stronger stimulated TNF-alpha responses. In ovarian cancer patients, patients' degree of social support has been related to higher cytotoxicity in the Natural Killer (NK) cells circulating in the mononuclear cells of the patient's peripheral blood. These peripheral-blood mononuclear cells (PBMC) are a critical component in the immune system, fighting infection and adapting to intruders. Higher cytotoxicity in the Natural Killer

(NK) cells was also found in immune cells that infiltrate tumours, referred to as tumour-infiltrating lymphocytes (TIL).

NKT cells are a rare group of lymphocytes, small white blood cells in the immune system exhibiting anti-tumour activity. Lamkin *et al* (2008) recently reported that greater social support is related to significantly higher levels of three distinct types of NKT cells in the tumours of ovarian cancer patients, and this may control the development of tumours.

Loneliness is being cited as causing low-grade peripheral inflammation which, in turn, is linked to inflammatory diseases such as diabetes, cardiovascular disease, and autoimmune disorders (e.g. rheumatoid arthritis, lupus). Attention has recently been drawn to the role of the cytokines macrophage migratory inhibitory factor (MIF) and the cytokine interleukin-6 (IL-6) as underlying this process. Interestingly, regular religious group participation is a significant predictor of elevated IL-6 levels and lower subsequent 12-year mortality.

Lack of social connection or loneliness is also associated with increased risk of cardiovascular disease. The neuropeptide oxytocin is increasingly considered the 'hormone of affiliation', released in plasma and cerebrospinal fluid in response to everyday aspects of human interaction such as somatosensory stimulation, hugging, touch, warm temperature – and it is also involved in feelings of trust and generosity. Oxytocin has recently been found to prevent detrimental cardiac responses including elevated resting heart rate, reduced heart rate variability, and reduced parasympathetic regulation of the heart in adult female animals exposed to social isolation. This may be one of the central mechanisms that underlie the relationship between social contact, cardiovascular disease or better cardiac function in humans.

### In our sleep

A study at the University of Chicago, using electrophysiological measures associated with REM and Non-REM sleep, found that loneliness predicts sleep efficiency – lonely people sleep less efficiently and spend more time awake. The authors conclude that sleep deprivation has profound autonomic, metabolic and hormonal effects and that this may account for differences between socially-isolated and connected individuals in morbidity rates. Poor sleep is now strongly linked to a wide variety of deleterious consequences. For example, a



What implications does the present rush for electronic networking have for traditional social relationships and networks?

study at Harvard Medical School concluded that even short-term poor sleep resulted in elevated levels of high-sensitivity CRP [C-Reactive protein] concentrations, a stable marker of inflammation that has been shown to be predictive of cardiovascular morbidity.

### Morbidity

Several decades of research has found that greater social contact is related to reduced morbidity while fewer contacts lead to increased morbidity. This relationship is valid, independent of the individual's earlier health status.

Rutledge *et al* (2008) recently reported that women with fewer social relationships experienced strokes at more than twice the rate of those with more social relationships after adjusting for covariates: "Smaller social networks are a robust predictor of stroke in at-risk women, and the magnitude of the association rivals that of conventional risk factors." And a study entitled *Social Interaction Improves Experimental Stroke Outcome* reported that social interaction reduces intraschismic CRP concentration and decreases the tissue damage caused by the obstruction of the inflow of blood during a stroke, in male and female mice. High CRP can predict future strokes in humans.

Loneliness is found to be a unique predictor of age-related differences in systolic blood pressure. And blood pressure for married adults – especially those happily married – declines more during sleep than for single people who may therefore be at much greater risk of cardiovascular problems. In one experiment, in which men were challenged in order to increase their blood pressure, it was found that blood pressure returned to baseline levels

more quickly in the men with more close friends.

In a rather crude way of looking at the benefits of having friends and families, Cohen *et al* (1997) exposed subjects to two rhinoviruses (RV39 and Hanks) and found that susceptibility to colds decreased in a dose-response manner: people with the most types of social bonds were the least susceptible, while those with one to three types of social relationships were over four times more likely to develop a cold than those people with six or more types. Others have found that loneliness and a small social network are independently associated with poorer antibody response to influenza vaccine. “The mere existence of social ties, independent of loneliness was associated with immune response to influenza vaccination,” concluded the study.

Cases of dementia are expected to double within a generation. A coalition of leading researchers recently warned the Government that new methods of prevention and treatment must be found “or the NHS won’t survive the next 20 years”. At the same time, however, research conducted by the Harvard School of Public Health has examined the influence of social integration, including frequency of social interaction, on changes in memory in 16,638 subjects aged 50 and older. Er-

tel *et al* (2008) concluded that memory loss among the least integrated declined at twice the rate as among the most integrated. Others report that the frequency of social interaction is inversely related to the incidence of dementia and may protect against dementia. Furthermore, the risk of cognitive decline and Alzheimer’s Disease was recently found to be more than double in lonely persons.

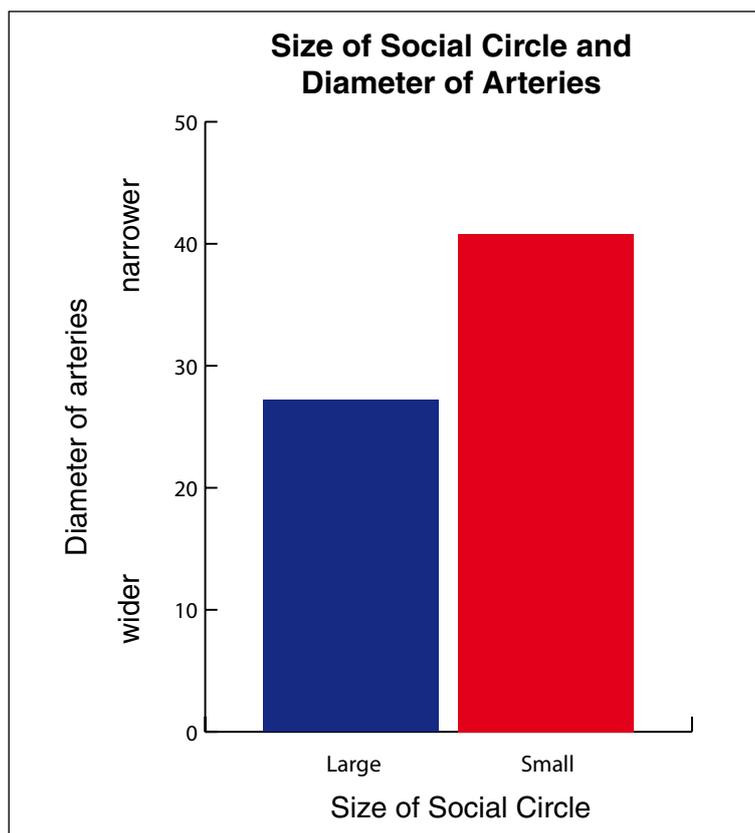
A positive relationship between the sheer amount of regular actual social contact and cognitive functioning has, however, been found in a variety of age groups including younger adults. Most interesting is the intervention study by Ybarra *et al* (2008) in which participants who interacted socially for only 10 minutes showed improved cognitive performance, performance equivalent to that displayed by participants engaged in so-called intellectual activities. The authors believe that not only do the results show that the effect is causal but that the process is very sensitive to only small amounts of social interaction. They conclude: “Social interaction directly affects memory and mental performance in a positive way.”

### Mortality

The European Prospective Investigation into Cancer and Nutrition recently found that early retirement may be a risk factor for all-cause and cardiovascular mortality in apparently healthy persons. Is there something about the lack of regular face-to-face social interaction that may explain this finding? Interestingly, a series of studies have continued to find a significant reduction in mortality, independent of confounding variables, in people who attend weekly religious services. However, simply showing up at church to ‘warm the pew’ may not be sufficient, as it is increasingly suggested that it is the underlying social interaction and connection amongst those who attend that influence mortality. And a 13-year prospective cohort study at the Harvard School of Public Health on the survival in older Americans concluded social activities are as effective as fitness activities in lowering the risk of death.

On the other side of the world, the Kom-Isse prospective cohort study in Japan finds that social networks are an important predictor of mortality risk for middle-aged and elderly Japanese men and women. Lack of social participation for men, and being single and lack of meeting close relatives for women, were described as independent risk factors for mortality. In the United States, a cohort study of women

**Figure 3.** Based on quantitative angiogram findings, subjects with smaller social networks had narrower arteries (mean angiogram stenosis value, 40.8 vs 27.2 for small vs. large social networks, respectively; ( $p < 0.001$ ) (adapted from Rutledge *et al.*, 2004).



with suspected coronary artery disease (CAD) found those with larger social networks had a consistent pattern of reduced CAD risk, including lower blood glucose levels, waist-hip ratios, rates of hypertension and diabetes, and less severe CAD as measured by differences in narrowing of the arteries (angiogram stenosis values 40.8 vs. 27.2 for small vs. larger social networks). Mortality rates showed a dose-response pattern: women with small social networks showing more than twice the death rate (see Figure 3) (Rutledge *et al.*, 2004).

### Marriage and cohabitation

The Office for National Statistics reports that the long-recognised protective effect of marriage against suicide has persisted over the past 25 years, despite changes in marriage patterns. Between 1983 and 2004, suicide rates for single people were around three times higher than for married people. For single women, the differential with married women widened from just over two times to three times. Unfortunately, our marriage rate is at an all-time low.

Simply being single was associated with a higher risk of mortality, a prospective cohort study of 94,000 Japanese people found, and it concluded that merely being unmarried constitutes a potentially adverse health effect. However, according to a study by the Institute of Public Health in Denmark, *cohabitation* was the main factor in regard to earlier death: individuals living alone experienced a significantly increased mortality compared to individuals living with somebody, married or not. Looking at males, a prospective birth cohort study of all-cause mortality from age 40 to 49 years found a strong protective effect at every age from being married compared with never being married or being divorced/widowed. Moreover, this effect occurred in a dose-dependent manner. By simply adding together the periods of time the man was married, the protective effects conferred by marriage were cumulative as were the deleterious effects of years being divorced. Most fascinating is that this cumulative effect is handed down from father to son, continuing to affect the rate of early death in subsequent generations and is "...significantly associated with mortality risk in a dose-response pattern....an accumulative effect as each of the three non-married generations added to an increased mortality risk." (Lund *et al.*, 2006).

Remaining single has however been



Studies in Japan indicate that social networks are an important predictor of mortality risk.

found to offer one particular health benefit to women. American criminologists report the decline in marriage is responsible for a decline in the murder rate, as husbands now have fewer opportunities to kill wives.

### Conclusion

While the precise mechanisms underlying the association between social connection, morbidity and mortality continue to be investigated, it is clear that this is a growing public health issue for all industrialised countries. A decade ago, a detailed classic study of 73 families who used the internet for communication, *The Internet Paradox*, concluded that greater use of the internet was associated with declines in communication between family members in the house, declines in the size of their social circle, and increases in their levels of depression and loneliness. They went on to report "both social disengagement and worsening of mood...and limited face-to-face social interaction ... poor quality of life and diminished physical and psychological health" (Kraut *et al.*, 1998).

Children are now experiencing less social interaction and have fewer social connections during key stages of their physiological, emotional and social development. An increasing proportion of men and women are living alone during their 'mating years' having far fewer social contacts. And as the greying of the population continues, the incidence and effects of social isolation are pronounced.

While physicians and their professional bodies regularly advise and admonish patients and the public on intimate matters including the number of sexual partners the individual has, encouraging people to 'interact more' or to pair-up for the sake of their health seems intrusive. Indeed enquiring about a woman's relationship status and pointing to the health risks of remain-

ing single, living alone would be considered impertinent – and politically inadvisable.

This however is precisely where biologists can play a pivotal role. By making the abstract concept of social connection and its effects more concrete and measurable, biology may finally provide the key to public awareness. Presiding over a growing body of evidence, we should now explain the true meaning of the term 'social networking'. At a time of economic recession our social capital may ultimately prove to be our most valuable asset.

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**Aric Sigman** is a Member of the IOB, Fellow of the Royal Society of Medicine and Associate Fellow of the British Psychological Society. He has travelled to various cultures, including North Korea, Bhutan, Tonga, Myanmar, Iran, Korea, Vietnam, Mali, Bolivia, Burkina Faso, Sumatra, Cambodia and Eastern Siberia to observe the influence of electronic media. Email: [aric@aricsigman.com](mailto:aric@aricsigman.com)

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