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John T. Cacioppo^a & Stephanie Cacioppo^b

^a Department of Psychology, University of Chicago,
Chicago, IL, USA

^b Department of Psychology, University of Geneva,
Geneva, Switzerland

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Commentary

The phenotype of loneliness

John T. Cacioppo¹ and Stephanie Cacioppo²

¹Department of Psychology, University of Chicago, Chicago, IL, USA

²Department of Psychology, University of Geneva, Geneva, Switzerland

Goossens' review (2012, this issue) nicely maps the progression of scientific research from its early focus on loneliness as a dysphoric state that results from the discrepancy between a person's ideal and actual social relationships to its current emphasis on the centrality of loneliness to our very nature as a social species, and he argues that developmental science throughout Europe has a great deal to contribute to our understanding of this construct. He concludes that psychologists should care about research on loneliness for five reasons: (i) it is a well-defined phenotype; (ii) it shows both high stability and individual differences in rates of change across years; (iii) it has adaptive value and evolutionary significance; (iv) it has a genetic substrate that is moderated by social environments; and (v) it has self-maintaining features that can lead to adverse mental health outcomes. Goossens' review is rife with information and ideas. We focus here on two additional important reasons and on the phenotype of loneliness.

Keywords: Gene \times Environment; Loneliness; Phenotype; Social connections; Social isolation.

Robert Weiss (1973) conceptualized loneliness as perceived social isolation, which he described as a gnawing, chronic disease without redeeming features. It perhaps is understandable how something as personally aversive as loneliness could be regarded as a weakness of character. However, evolutionary time and evolutionary forces operate at such a different scale of

Correspondence should be addressed to John Cacioppo, Department of Psychology, University of Chicago, 5848 S. University Ave, Chicago, IL 60637, USA.

E-mail: cacioppo@uchicago.edu

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organization from what we experience in everyday life that personal experience is not sufficient to understand the role of loneliness in human existence.

Meta-analyses of the odds ratio for increased mortality for loneliness is 1.45—larger than found for social support, marriage, and physical activity and approximately double the odds ratio for increased mortality for obesity and more than four times the odds ratio for air pollution (Holt-Lunstad, Smith, & Layton, 2010). Not only is the effect size large, the condition is surprisingly prevalent. Although most people are not chronically lonely, representative samples in the USA suggest that more than 20% of adults experience frequent or intense loneliness at any given time, with one recent national sample suggesting this rate could exceed 30% (Edmondson, 2010). Social networking does not appear to be the answer either. Technology has made it possible for people to connect in ways never imagined, and people worldwide have jumped at the opportunity. The number of friends one has on social networking sites is associated with lower levels of loneliness, but these friends typically are made in face-to-face interactions rather than online. Coney (2011) found that a higher proportion of face-to-face contacts with confidants predicted lower levels of loneliness, whereas a higher proportion of contacts with confidants through social networking sites predicted higher levels of loneliness.

Research over the past decade suggests a very different view of loneliness than suggested by personal experience, one in which loneliness serves a variety of adaptive functions in specific habitats. Loneliness heightens sensitivity to social threats and motivates the renewal of social connections; increases depressive symptomatology, tonic sympathetic tonus, HPA activation, sleep fragmentation, and genes regulating leukocyte activation and cellular response to oxidative stress; and decreases inflammatory control, immunity, dopaminergic brain activity in response to pleasant social encounters, and the expression of genes regulating glucocorticoid responses and Type 1 interferon innate antiviral responses (Cacioppo, Hawkley, Norman, & Berntson, 2011; Cole, Hawkley, Arevalo, & Cacioppo, 2011). Together, these effects can contribute to higher rates of morbidity and mortality seen in older adults.

The phenotype of loneliness is more nuanced than it may appear at first glance as well. The phenotypic expression of loneliness has been described as a strong sense of social pain, emptiness, isolation, sadness for lack of confidants, unimportance and worthlessness (Weiss, 1973). Quantitative analyses have revealed three basic dimensions underlying this phenotype, reflecting the degree of isolation (or connection) in three domains: intimate attachments, face-to-face relations, and social identities (Hawkley, Browne, & Cacioppo, 2005). These three dimensions are correlated but statistically and functionally separable, and surprisingly generalizable. This dimensional structure has been identified in men as well as women; African Americans, Euro Americans, and Latino Americans; and in young adults as well as

older adults in the USA (Hawkley et al., 2005) and in China (Hawkley, Gu, Luo, & Cacioppo, 2012).

The first dimension is *intimate isolation/connection*, or what Weiss (1973) termed emotional loneliness, and it refers to the perceived presence/absence of someone in your life who serves as a nurturing confidant, someone who affirms your existence. In a population-based study of middle-age and older adults, the best predictor of intimate isolation (net the other two factors that were identified) was marital status: participants who were married were, on average, lower in intimate isolation than were participants who were unmarried (Hawkley et al., 2005).

This facet of the phenotype of loneliness, with its emphasis on emotional aspects of loneliness and intimate connectedness, may be based on heritable differences in sensitivity to the pain of social disconnection (Cacioppo & Hawkley, 2009). As Goossens (2012, this issue) notes, these individual differences can serve an important function in an evolutionary timescale. For instance, individuals who are relatively insensitive to the pain of social disconnection may be more likely to serve as explorers but their insensitivity to social connection may not compel them to return to share their discoveries. Individuals who are sensitive to the pain of social connection, in contrast, may be more likely to remain in or return to the group and contribute to the protection and maintenance of the group, but they may be less likely to make solitary journeys that reveal new territories, threats, or opportunities. Both types of predispositions can be important.

What evidence is there that the heritability of loneliness reflects, at least in part, individual differences in sensitivity to social disconnection? Relevant evidence is available from a surprising source: Hofer's (2009) research on the selective breeding of rats. A well-characterized response to maternal separation is the separation cry. In the rat, the separation cry is in the ultrasonic range (40–45 kHz). These ultrasonic vocalizations (USVs) to isolation are attenuated in a dose-related fashion by anxiolytics that act on benzodiazepine and serotonin receptors and are exaggerated by anxiogenics such as the benzodiazepine receptor partial inverse agonist FG7142.

Neuroanatomical studies reviewed by Hofer (2009) point to the periaqueductal grey area (PAG) as a neural substrate for these USVs in rats and the hypothalamus, amygdala, thalamus, and hippocampus and cingulate cortex as the neural substrates for isolation calls in primates. The recruitment of the PAG in mechanisms related to social isolation makes sense as PAG is part of a circuit that controls nociceptive neurons in the dorsal horn of the spinal cord, with stimulation of the PAG suppressing pain transmission via the release of endogenous opioids during painful experiences (MacDonald & Leary, 2005). For instance, research shows that lesions to the lateral or ventrolateral PAG in rat pups can disrupt the decreased pain sensitivity following social isolation compared to that experienced in pups assigned to a sham (or “placebo”) lesion condition

(Wiedenmayer, Goodwin, & Barr, 2000). Interestingly, with its direct connections with regions of the limbic system (e.g., cingulate cortex) and with vasopressin-rich brain regions that are known to be important in maternal bonding, PAG has also been shown to be involved in attachment (MacDonald & Leary, 2005; Ortigue, Bianchi-Demicheli, Patel, Frum, & Lewis, 2010). Along these lines, Hofer uses the concept of attachment to describe the emotional expression represented by the USVs and the re-establishment of the social bond by the maternal search for, renewed contact with, and comfort response of the rat pup.

Some rat pups, who might be characterized as sensitive to separation, cry frequently (albeit ultrasonically) when isolated, whereas others are less sensitive to separation and show less distress when isolated. Hofer and colleagues selectively bred adult rats that, as rat pups, showed either high or relatively low rates of USVs to separation (Hofer, 2009). After 25 generations of selective breeding, differences in behaviour between the two lines of rats were reminiscent of some of the differences observed in humans who are high or low in loneliness: the high, relative to low, USV line showed more distress to isolation as an infant; greater latency to play as an adolescent; and greater depression-like behaviours, greater anxiety-like behaviours, greater latency to social interactions, greater startle, and diminished learning as an adult. That is, the high USV line was anxious and passive, whereas the low USV line was exploratory, active, and aggressive.

This work, then, supports a link between loneliness and attachment processes and points to a specific *aspect* of the phenotype (sensitivity to isolation) and evolutionary mechanisms for this phenotype. Note, however, that in this context the mother–infant attachment *builds* on heritable differences in sensitivity to isolation rather than the pain of isolation resulting from poor infant attachment behaviours by the mother.

The second phenotypic dimension is *relational isolation/connection*, or what Weiss (1973) termed social loneliness. It refers to the perceived presence/absence of quality friendships or family connections. The best predictor of relational isolation was the frequency of contact with friends and family: participants who had frequent contact with friends and family were lower in relational isolation even after statistically controlling for the two other loneliness factors (Hawley et al., 2005).

The relational connectedness aspect of the phenotype of loneliness may have a different evolutionary basis than the intimate connectedness aspect. For instance, loneliness not only serves to signal the prospect that our social connection is at risk or absent and to motivate us to repair or restore the safe, collaborative social surround we need to ensure a genetic legacy, but it may also provide incentives to become more compassionate and empathic members of our social species. Consider the contemporary practice of time-out. When a child acts selfishly or socially inappropriately, a common practice is to isolate the child from others. This enforced isolation is

typically painful for the child and may be associated with displays of sadness or general negative affect, which we noted above serves as an appeal for connection and support by anyone in the vicinity. Upon reintegration to the group following the time-out, the child tends to act in a more empathetic, less narcissistic fashion—that is, the existence of the aversive state of loneliness contributes to our socialization and culture.

Although time-out is a recent innovation, it is illustrative of a more general principle in which an individual in a social setting who is made to feel isolated is compelled to change his or her behaviour toward others. The “silent treatment” between close social others, workplace expulsion, teasing, being excluded or ignored in social circumstances, and countless other passive or active rejection behaviours, whether enacted for virtuous or malicious reasons, are potent elicitors of social pain (Williams, Suchy, & Rau, 2009) and can also serve to promote other-oriented social motives. Evidence of shunning and ostracism can be found in nonhuman social species as well as in various cultures across human history. Ostracism in most social species is associated with an early death (Williams, 2001). Because humans need to be able to work together to survive and prosper, the effects of time-out, shunning, and related methods of interpersonal rejection on people’s social skills (e.g., reduced selfishness, increased perspective taking and empathy) benefit the individual and contribute to social adhesion and resilience.

Humans are especially adept in observational learning—extracting information about the environment based on their observations of the costs and benefits of those with whom they are connected or about whom they care. Social learning, in turn, promotes the development of common knowledge and practices, that is culture, adding to the centripetal forces banding individuals together to form adaptable, co-operative groups (Rendell et al., 2010). The effect of loneliness on people’s attention to interpersonal information may, therefore, have the additional benefit of promoting social learning.

The third phenotypic dimension is *collective isolation/connection*, an aspect that Weiss (1973) did not identify in his qualitative studies. Collective isolation refers to the perceived presence/absence of a meaningful connection with a group or social entity beyond the level of individuals (e.g., school, team, nation). The best predictor found in middle-aged and older adults for collective isolation was the number of voluntary groups to which participants belonged: the more voluntary associations to which participants belonged, the lower their collective isolation, again even after statistically controlling for the two other factors (Hawkey et al., 2005).

In the human pair-bond and nuclear family, the members are part of a larger collective within which the nuclear family is fully integrated. Indeed, the human pair-bond may have evolved hand in hand with the group. For

instance, heterosexual pair-bonding in humans raises the certitude of paternity, thereby increasing the parental investment in dependent offspring. In addition, it lessens rivalry for sexual partners among males, with the consequent reduction in sexual rivalry lessening the competition among males, promoting co-operation in hunting and warfare, and altering the organization and operation of the population to make it more resilient. As de Waal and Pollick (2005) note: “Human families are part and parcel of the society . . . In evolutionary terms, there first must have been the larger society, within which developed the human family” (p. 34).

In sum, natural selection operates on phenotypes. It therefore can be useful to articulate the full phenotype of loneliness and to consider its adaptive function within an evolutionary timescale. Specifically, an explication of the phenotype of loneliness and a description of the adaptive function each aspect of this phenotype might be serving may help us understand the genetic contributions to loneliness and the nature of the interactions between these genes and the social environments in which these genes are expressed.

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