



Network cultivation, diurnal cortisol and biological ageing: The rejuvenation hypothesis[☆]

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ABSTRACT

A stronger motivation to cultivate social ties in older adults (ages range from 62 to 86 years) has been associated with a cortisol profile similar to that observed in undergraduate students, who are decades younger. We have shown the cultivation of social networks buffers against increases in diurnal cortisol common in old age. Cortisol is crucial for the response to stress and the process of ageing, and a recent study has demonstrated that a lower cortisol level is associated with longevity. We link the findings of social network cultivation and cortisol profile to the processes of biological ageing through DNA telomere length. Telomeres are repeated DNA sequences that cap and protect the ends of chromosomes, and telomere length is considered a potential biomarker for biological age because it is closely related to the cellular process of ageing and chronic stress and is inversely related to chronological age. Studies examining biological ageing have shown an association between an altered cortisol profile and telomere length dynamics. Together, these findings on social networks, cortisol profiles and telomere length suggest that seniors who are motivated to maintain social ties are biologically younger. We therefore propose the ‘rejuvenation hypothesis’, which posits that seniors with a stronger motivation for social network cultivation are biologically younger, as measured by cortisol levels and telomere length, than their peers who are less motivated to pursue social relationships. This idea suggests a new perspective and potentially fruitful direction for geriatric research. The focus on social network cultivation adds an important psychosocial dimension to rejuvenation therapies that so far have been dominated by biomedical approaches. The rejuvenation hypothesis also has important implications for social policy by supporting the viability of promoting network cultivation among the elderly to facilitate healthy ageing.

Social network cultivation, diurnal cortisol and biological ageing

Cortisol profiles and biological ageing

The hypothalamic-pituitary-adrenocortical (HPA) axis mediates among brain activity and the major physiological systems of the body. It is therefore crucial for adjustments to stressful challenges and also the process of ageing [1]. The ageing of the HPA axis is one of the key factors driving immunosenescence [2], and a recent study has demonstrated that a lower cortisol level is associated with longevity [3]. Although the importance of the HPA axis in the process of ageing is widely appreciated, how ageing alters the function of this neuroendocrine axis in humans is not completely understood. Convergent evidence has shown that a precise characterisation of age-driven changes in the function of the HPA axis requires accounting for the influences of the biological processes of ageing, resilience and risk factors [4].

Although a conceptual model linking ageing, stress and resilience has recently been proposed [5], it focuses primarily on the effect of chronological age without giving due attention to markers of biological ageing. The use of markers of biological ageing has become widely accepted and increasingly crucial for understanding the effect of ageing on health status [4,6]. In the last decade, telomere length (TL) has emerged as one of the most researched biomarkers of ageing because it is closely associated with the cellular process of ageing [7] and chronic stress [8].

Telomeres are the repeated DNA sequences that cap and protect the ends of chromosomes. The TL shortens with each cycle of cell replication, and such attrition ultimately leads to replicative senescence [7]. TL is inversely associated with chronological age (correlation coefficients ranging from -0.5 to -0.6 ; [9]) and has stronger associations with functional and health statuses than chronological age [4]. There is ample evidence showing that telomere shortening is associated with

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exposure to chronic stressors (e.g., caregiving [10]; perceived stress [11]; cumulative lifespan adversity [12]; and marital disruption [13]), while longer TLs are associated with more years of healthy life [14]. Importantly, a higher nocturnal cortisol level and a flatter diurnal slope have been found to be associated with shorter TL in older women [15]. This association can be explained by the suppressive effect of cortisol on the activity of telomerase, an enzyme that protects telomeres against attrition, via a reduction in the transcription of the human telomerase reverse transcriptase [16]. Although most studies have focused on the negative health implications of telomere shortening, the potentially positive effects of longer TL should not be overlooked. Taken together, recent data suggest telomere dynamics could be the common pathway by which chronic stress and ageing converge to affect the health status of seniors. This idea raises the important question of whether the ageing of the HPA axis is associated with TL shortening. Put differently, the pressing question is whether a rejuvenated HPA axis in old age is associated with longer TL.

The role of social network cultivation in cortisol profiles and biological ageing

In the context of recent findings about the HPA axis and telomere shortening, the findings from two of our previous studies have become relevant [17,18]. The first study examined the novel construct of network cultivation (NC), which is defined as the time and effort invested in cultivating social ties with family, relatives, friends and neighbours. We found an inverse relationship between the NC score and diurnal cortisol level/slope in healthy Chinese elders [17]. The second study reported the diurnal cortisol profile in a group of undergraduates [18]. As shown in Fig. 1, older adults with higher NC scores tended to exhibit a lower diurnal cortisol level and a more effective decline compared to the undergraduates. To examine the differences in cortisol levels among the seniors, who were grouped into four quartiles based on NC scores, and undergraduates at each of the four sampling time points, we computed a series of t-tests. As illustrated in Table 1, the difference in cortisol levels between seniors and undergraduates was more salient at 6 and 12 h after waking. In particular, seniors with higher NC scores tended to exhibit an effective deactivation of the HPA axis, similar to what was observed in the undergraduates.

Table 1
Comparison of mean diurnal cortisol levels in undergraduate participants and seniors in NC quartiles.

	Hours Post-Waking			
	0	3	6	12
Seniors 1st Quartile	9.98 (0.87)	5.90 (0.41)	4.57 (0.42)*	4.02 (0.29)**
Seniors 2nd Quartile	8.91 (0.67)	4.48 (0.53)	4.16 (0.38)	3.23 (0.32)*
Seniors 3rd Quartile	7.33 (0.65)	3.36 (0.24)	2.85 (0.31)	1.45 (0.14)
Seniors 4th Quartile	7.04 (0.65)	3.60 (0.27)	2.94 (0.24)	1.54 (0.10)
Undergraduate Participants	7.91 (0.89)	4.57 (0.59)	3.03 (0.45)	2.06 (0.34)

Note: Means of Network Cultivation (NC) scores of the each of the four quartiles are 6.69, 9.46, 11.56 and 14.23, respectively. T-tests (one-tailed) were performed on the differences between mean cortisol levels in seniors with low NC scores and mean cortisol levels in undergraduates. *p < .05; **p < .001. SEs are in parentheses.

The rejuvenation hypothesis

Because a ‘younger’ cortisol profile, as shown in Table 1, is likely to lead to increased TL through decreased inhibition of telomerase activity, we posit the cultivation of social networks could lead to younger biological ages for seniors. In other words, seniors with a high motivation to cultivate their social networks are likely to be biologically younger, as measured with cortisol levels and telomere length, than their peers who have less motivation for network cultivation. The rejuvenation hypothesis integrates psychoneuroendocrine research with work on biological ageing and could have important implications for rejuvenation therapies.

Cortisol profiles in older adults

The validity of the rejuvenation hypothesis rests on the assumption that the function of the HPA axis declines with age. Such a decline is marked by a higher diurnal cortisol level and a flatter diurnal slope

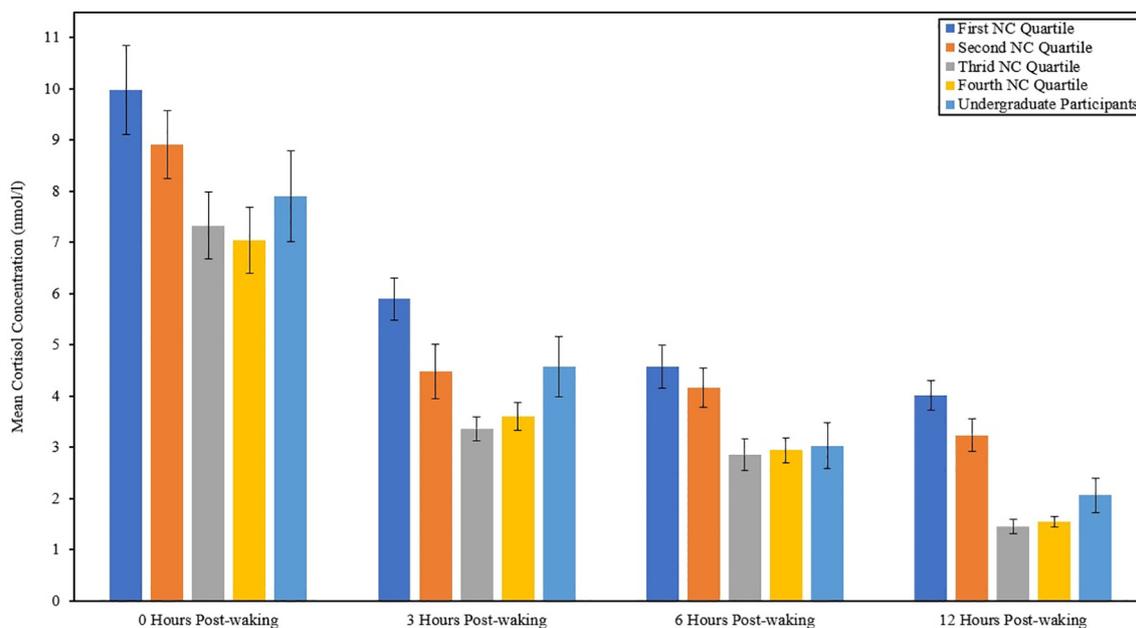
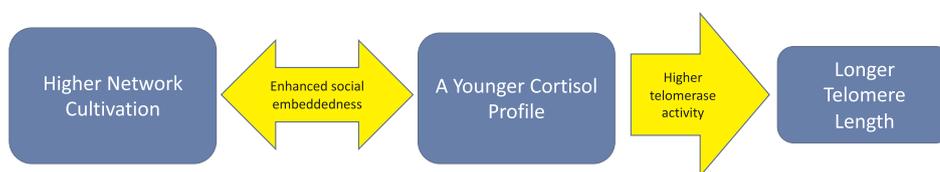


Fig. 1. Diurnal cortisol profiles (means with SE bars) after waking in healthy seniors (n = 78) and undergraduates (n = 51). Seniors are classified into four quartiles based on NC score. The mean age of the seniors was 73.09 years (range: 62–86 years), and the mean age of the undergraduate sample was 20.90 years (range: 18–29 years).



cultivate their social network.

(e.g., [17]), which is supported by recent evidence (e.g., [5,19,20]) and illustrated in Fig. 1. The increase in diurnal cortisol can be attributed to the impairment of negative feedback along the HPA axis [19] or a reduction in the number or sensitivity of mineralocorticoid and glucocorticoid receptors in the older age groups [5]. The health effect of hypercortisolism should not be underestimated because chronically elevated cortisol levels lead to atrophy of the hippocampus and accelerate cognitive decline in old age [21]. However, as illustrated in Fig. 1, the increase in diurnal cortisol in old age is buffered by NC. The cortisol profiles in seniors with higher NC scores were similar to profiles of a much younger age group. Although telomerase activity is also regulated by sex hormones and growth factors (e.g., [22,23]), there is no evidence showing that the cortisol-TL association is determined by these hormones.

Network cultivation and healthy ageing

Chinese elders who spent more time and effort cultivating their social relationships with family, relatives, friends and neighbours had lower levels of diurnal salivary cortisol and steeper diurnal declines [17]. This diurnal pattern was similar to a younger participant group [18]. These findings indicate the importance of NC in maintaining a ‘biologically younger’ cortisol profile and suggest possible implications for a range of both mental and physical health outcomes. NC is functionally similar to another novel motivational construct, the Reaffiliation Motive (RAM). The RAM denotes the motivation to reconnect in response to perceived social isolation from disruptions of social ties and is thus particularly relevant to old age [24]. Although no evidence has yet linked these two novel concepts, reconnection implies the investment of time and effort to re-establish and maintain social ties, which is similar to what the NC models. The RAM and NC might also be activated by the same trigger of loneliness prevalent among older people [25] and particularly among Chinese elders [26].

Conclusions and implications of the rejuvenation hypothesis

A meaningful pattern of relationships among NC, diurnal cortisol profiles and telomere length supports a rejuvenation hypothesis: a higher NC score is associated with a younger cortisol profile, which is itself associated with longer TL (Fig. 2). Due to the scarcity of longitudinal data in general, the issue of causality has not yet been adequately addressed. It is therefore possible that a younger cortisol profile and the associated longer TL could also enhance NC. Better adjusted and more functionally capable seniors are likely to be more motivated to cultivate social ties. The associations of cortisol, behaviours and cognition with NC could potentially be effective points of focus for social policy theorists and targets for community intervention [17,27]. The focus on NC adds an important psychosocial dimension to rejuvenation therapies that so far have been dominated by biomedical approaches that use either cortisol/dehydroepiandrosterone [2] or telomere/telomerase [28] as the therapeutic target. Promoting NC might complement the biomedical approaches and augment any beneficial effects. This idea is supported by recent evidence showing a positive effect from lifestyle change intervention programs on telomerase activity (e.g., [29,30]).

Considering the theoretical importance of the construct of NC in

Fig. 2. The Rejuvenation Hypothesis posits that healthy seniors who are motivated to cultivate their social ties are biologically younger than their peers, where biological age is measured by cortisol profiles and telomere length. Seniors with high NC scores have a ‘younger’ cortisol profile and likely longer overall telomere length compared to their peers who are less motivated to

modulating biological ageing via the HPA axis, further research using longitudinal experimental designs is warranted. These longitudinal experimental designs could address the question of whether a younger cortisol profile leads to longer TL. Such experiments will generate more robust data to address causality and justify the implementation of community interventions. Because both cortisol and TL are sensitive to a wide range of biological and psychosocial factors (e.g., [23,31]), an effective control for the influences of these confounding variables or covariates will be necessary to assess any effects attributable primarily to NC. Due attention should also be given to the influences of genetic factors on TL, as heritability of TL ranges from 36% to 90% and linkage to chromosomes 12 and 14 has also been reported [32,33]. These methodological challenges are immense but surmountable.

Conflict of interest

None to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2018.09.041>.

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