PSYCHOLOGICAL HEALTH AND WELL-BEING: A RESEARCH AGENDA FOR THE EASTERN TOWNSHIPS

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Abstract
Well-being is an important concept that has received increasing research attention in recent years. A related concept, psychological health and well-being, introduces the notion that mental health is a key aspect of well-being. Following a review of current conceptualizations of well-being and their links to psychological well-being, this paper presents current evidence documenting how well-being is associated with important outcomes across a variety of life domains, including work, social and community life, and health. Planned and ongoing research conducted by members of the Psychological Health and Well-being research cluster at Bishop's University is then briefly summarized and its importance for the people and communities of the Eastern Townships is highlighted.

Résumé
Le bien-être est un concept important qui attire de plus en plus l'attention des chercheurs. La santé mentale et le bien-être, un concept qui lui est apparenté, permet d'affirmer que la santé mentale joue un rôle clé dans la présence d'un sentiment de bien-être. À la suite d'un survol des conceptualisations actuelles du bien-être et des liens qu'elles entretiennent avec le bien-être psychologique, cet article rendra compte des différents projets de recherche en cours qui documentent la façon dont le bien-être est intimement lié aux issues d'une variété d'aspects de la vie, notamment la vie professionnelle, sociale et communautaire ainsi que la santé. Nous brosserons ensuite un portrait sommaire des projets de recherche en cours ou prévus dirigés par les membres du groupe de recherche sur la Santé mentale et le bien-être, basé à l'Université Bishop's. Enfin, l'impact de ces projets de recherche sur la communauté des Cantons-de-l'Est sera brièvement décrit.

Whether conceived of as a momentary state or as an ongoing process of growth and adaptation to changing life circumstances, well-being has become the focus of much research in recent years. Quality of life, wellness, happiness, and thriving are related terms used by researchers that similarly convey the notion of experiencing life as something positive and satisfying. The term psychological health and well-being further delineates this idea by suggesting that psychological health is central to the experience of well-being.

In 2009, Bishop's University identified psychological health and well-being as one its four strategic research areas. This particular research focuses on finding ways to improve the health and well-being of individuals and communities. The Psychological Health and Well-being Research Cluster is a research group formed of members from the fields of Social Sciences, Humanities, Natural Sciences, and Business whose activities are aligned with this aim. Their overall objective is to produce knowledge regarding how people and groups within the community can pursue their goals in ways that support health and well-being, and to identify the tools that will help them achieve this.

As the recently appointed Tier II Canada Research Chair in Health and Well-being for the Psychological Health and Well-being research cluster at Bishop's University, it is my pleasure to have this opportunity to present and discuss this important topic. In this paper I will outline current conceptualizations of psychological health and well-being, and discuss the reasons why it is an important goal for both individuals and communities. More specifically, I will discuss the possible ways that the recently created Psychological Health and Well-being Research cluster at Bishop's University proposes to study the means to ensure that the people of the Eastern Townships thrive and remain healthy and vibrant.

Conceptualizing Well-being

Although the term "well-being" is purported to date back to the early 1600's (Online Etymology Dictionary), it is only in recent years that the concept of well-being has become ubiquitous within the research literature. This may be due in part to its connections with health and health-care as a desirable outcome of treatment interventions for mental and physical health issues. Indeed, a survey of the scholarly health-related research literature demonstrates this popularity with almost 475,000 citations indexed by this term in the past 5 years alone. The term well-being is, however, also used widely outside of health contexts to describe the overall quality of life experienced by both individuals and communities with respect to their emotional, social, and financial status. Whether used in a specific or general context,

researchers generally agree that well-being refers to a subjective state characterized by a predominance of positive feelings.

Early conceptualizations of well-being were focused on the absence of distress (McDowell, 2010), whereas recent views have shifted to a more comprehensive focus on the positive characteristics and strategies involved in the development and experience of well-being. Fuelled by the growing interest in positive psychology—a sub-discipline that concentrates on understanding human flourishing and growth—scholars in Psychology have proposed several detailed but divergent models of well-being. These different conceptualizations can be viewed as falling into one of two competing camps. The first camp views well-being from a hedonistic perspective, focusing primarily on the role of positive and negative feelings in the experience of well-being. The second camp approaches well-being from a dynamic eudaimonic perspective, rejecting the notion that positive feelings alone indicate well-being and focusing instead on the active, growth-related aspects of well-being (Waterman, 1993).

From the hedonic tradition, well-being is closely aligned with the ancient Greek Epicurean conceptions of the purpose in life and the nature of living the "Good Life" (Waterman, 1993, 2008). The ultimate goal in life, from the view of the hedonist, is to maximize pleasure—"hedonia"—and minimize pain. Accordingly, achieving hedonia becomes the ultimate purpose in life, regardless of how feelings of pleasure are achieved. One model that views well-being from this hedonic perspective proposes that well-being is comprised of two general components: an emotional component characterized by high levels of positive feelings and low levels of negative feelings, and an evaluative component that includes overall satisfaction with one's life and satisfaction with specific and important life domains such as work, personal life, family life, etc. (Ryan & Deci, 2001). Because evaluation of both of these components is completely subjective, some researchers have adopted the term "subjective well-being" to describe this particular hedonic view (Diener, 1984; Diener, Suh, Lucas & Smith, 1999). Consider the following two examples that illustrate the hedonic view of well-being. An individual who has a modest standard of living that meets basic needs but who values and enjoys connections with a large extended family rates subjective well-being as relatively high because of the pleasure obtained from regular and meaningful contact with her or his family-based social network. Contrast this to someone who is the CEO of a large corporation and who enjoys a standard of living that most people can only dream of, but who has few if any social contacts with whom he or she can share his or her successes. If this CEO values having a successful career, a solitary lifestyle and enjoy-

ing the finer pleasures in life that only money can buy then he or she may also rate his or her subjective well-being at the same level as the person with only modest means who has many social contacts. These examples highlight one of the major criticisms of this hedonic model of well-being, namely that it provides a descriptive account of well-being without identifying the sources of well-being or explaining why individuals experience different levels of well-being.

An alternative and rivalling view of well-being, the eudaimonic perspective, also has its roots in classical Greek teachings. However, this eudaimonic approach favours the ethics of Aristotle over those of his pleasure-seeking contemporaries. Rather than the pursuit of pleasure, the eudaimonic view proposes that well-being arises when one pursues goals that are aligned with the authentic self, or *daimon*. Indeed Aristotle, in his *Nicomachean Ethos* (Trans. T. Irwin, 1985), proposed that eudaimonia was not a subjective but in fact an objective state that derived from contemplating the best within oneself and personal excellence (Waterman, 2008). Modern scholars who subscribe to this particular view of well-being take this one step further by focusing on how one might not just contemplate but also act upon these personal contemplations. From this view, then, well-being is an emergent property of engaging in pursuits that lead to personal growth and that develop one's potential. Rather than focusing on achieving end states of satisfaction and positive feelings, in other words happiness, the eudaimonic approach to well-being is dynamic and process-focused and highlights the importance of being engaged in meaningful goals in life for enhancing well-being. In short, its focus is more on the process of flourishing rather than simply feeling good.

One popular model of well-being founded on this eudaimonic perspective is that of *psychological well-being* proposed by Ryff and colleagues (1989; Ryff & Keyes, 1995). Psychological well-being is proposed to be a state of optimal psychological functioning comprised of multiple dynamic dimensions. The six core dimensions suggested to be essential for optimizing quality of life are 1) self-acceptance, 2) autonomy, 3) environmental mastery, 4) personal growth, 5) purpose in life, and 6) positive relations with others. The latter three dimensions in particular are deemed to capture the essence of eudaimonic well-being as being dynamic and action-oriented by focusing on purposefully pursuing personally meaningful goals and cultivating rewarding relationships. Although this newer view of well-being has now been around for two decades, research has predominately focused on hedonic models of well-being. It is only very recently that researchers have begun to integrate the two theoretical traditions (Keyes, 2006).

Apart from the subjective/objective distinction, hedonic and eudaimonic perspectives of well-being also differ with respect to their capacity to explain why someone may or may not be experiencing a certain level of well-being. Recall the example given earlier contrasting two individuals with very different life circumstances who nonetheless might report experiencing high levels of well-being. From the hedonic perspective, both individuals experience positive feelings and satisfaction with their life circumstances and are therefore happy. But the reasons *why* they have positive feelings and satisfaction are not further explained apart from identifying that they both experience positive feelings and life satisfaction. From the eudaimonic perspective, having many rewarding friendships and family relationships contributes to the well-being of the individual living by modest means, whereas being engaged in a meaningful and purposeful career similarly enhances the well-being of the second individual. Although both perspectives have merit, the eudaimonic perspective offers a more comprehensive theoretical view of the components of well-being which is essential in order to advance our understanding of how people can enhance their quality of life.

To summarize, research on well-being has distinguished two traditions based on early Greek writings on how to live the Good Life: 1) hedonic well-being, which focuses on feelings of pleasure and satisfaction and which can be thought of as *emotional well-being* (Keyes, 2007), and 2) eudaimonic well-being, which embodies the notion of personal growth and realizing one's potential as being essential to living the Good Life. Although the hedonic approach has tended to dominate research on well-being, eudaimonic perspectives are receiving increasing attention (see Deci & Ryan, 2008 for an overview) as they provide a comprehensive view of how and why people may experience different levels of well-being, as well as how life goals may play a role in the development of well-being. Nonetheless, there is considerable overlap between the two: fulfilling one's potential may indeed lead to increased feelings of happiness, making it more likely and practical to think of each type of well-being as running in tandem with one another (Biswas-Diener, Kashdan & King, 2009; Kashdan, Biswas-Diener & King, 2008), rather than being truly separate and distinct.

Psychological Health and Well-being

A concept related to well-being, psychological health is currently defined as including more than just the absence of mental illness. This term embodies the notion of health that was first redefined by the World Health Organization in 1948 to mean "a complete state of physical, mental, and social well-being and not merely the absence

of disease or infirmity" (World Health Organization, 2002). In Canada, the term health is often viewed from a public health promotion perspective which conceptualizes health as "the capacity of people to adapt to, respond to, or control life's challenges and changes" (Frankish, Green, Ratner, Chomik & Larsen, 1996). Implicit within this conceptualization is the idea that self-regulation—the ability to control and regulate one's actions—is central to how people improve, maintain and manage their health and well-being. We will return to a discussion of the role of self-regulation for health and well-being later in this paper.

Psychological health is often seen as synonymous with mental health, a term that was initially defined in terms of the absence of depression and anxiety and other psychopathological states (Westerhof & Keyes, 2010). However, much like the way we currently view "health," both mental health and psychological health are now more routinely taken to imply positive states of psychological functioning rather than the absence of mental illness or disorder. Keyes (2007) further proposes a eudaimonic view of mental health, suggesting that it should be viewed as flourishing because "the absence of mental illness is not the presence of mental health" (Keyes, 2007, 95). In keeping with this view, the recent World Health Organization (2005) definition of mental health as "a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" reflects this shift in understanding the determinants and necessary conditions of mental health. In fact the WHO (2005) has identified three core components of mental health within this definition: (1) well-being, (2) effective functioning of an individual, and (3) effective functioning for a community. Beyond stipulating that mental health includes well-being, this perspective proposes that not only effective individual functioning but also community functioning are essential for mental or psychological health. The implications of this particular view will be discussed further in this paper as we explore what psychological health and well-being may mean for the people and communities of the Eastern Townships.

As can be seen from the above discussion, the concept of mental or psychological health embodies several of the key aspects of well-being as defined by the two prevailing well-being traditions. Emotional or hedonic well-being is perhaps best reflected by the first component, whereas the core elements of eudaimonic well-being are captured by the second, that is, the notion that realizing one's potential and functioning effectively in the world is key to the experience of well-being. Given the conceptual overlap among the terms mental or psychologi-

cal health and well-being, using the term psychological well-being seems an appropriate way to capture the essence of both these components which of course are inextricably linked.

Why is 'Psychological Health and Well-being' worth studying?

The previous discussion focused on unpacking the term psychological health and well-being while emphasizing the distinctions among the two prevailing traditions that have been applied when studying well-being in general. Although it is clear that well-being, and especially psychological health and well-being, is much more than simply "happiness," the question remains as to why we need to study well-being at all. What can be gained by researching psychological well-being, its antecedents, correlates and consequences? In this next section, I will argue that a research program focused on improving our understanding of the development and sustainment of psychological health and well-being is both necessary and important for individuals and communities, and that psychological health and well-being is, as some researchers have suggested, functional beyond just "feeling good" when things go well (Oishi, Diener & Lucas, 2007). To ignore this important aspect of life in favour of apparently more concrete or practical concerns is ostensibly short-sighted and problematic for a variety of reasons.

First, we will consider the research that has identified some of the consequences of having high and low levels of psychological well-being. Apart from experiencing higher levels of positive affect or "happiness," people with high levels of psychological well-being tend to do better in life. That is, well-being is not just a potential outcome of life going well, but when achieved can be a precursor of many important outcomes we associate with life going well. For example, a recent review of over 200 papers found that compared to people low in well-being, people with high levels of well-being or "happiness" fared better in important life domains such as work, social and community life, and health (Lyubomirsky, King & Diener, 2005). People with high well-being are more likely to graduate from college and then secure better jobs (Lyubomirsky et al., 2005). They hold more prestigious jobs (Roberts, Caspi & Moffitt, 2003), are viewed more positively by their supervisors (Cropanzano & Wright, 1999), and even make more money (Lyubomirsky et al., 2005). They are also more productive, have lower levels of absenteeism, and are conscientious employees (Lyubomirsky et al., 2005).

In the social and community domain, having high levels of happiness is linked to a greater likelihood of being married (Lucas, Clark, Georgellis & Diener, 2003) and being satisfied with marriage afterwards

(Lyubomirsky et al., 2005). Higher levels of well-being are also linked to greater community involvement and volunteering (Lyubomirsky et al., 2005; Oishi et al., 2007). One reason for these observed social benefits is that people who experience high levels of well-being are known to exhibit adaptive social behaviors such as being more socially expressive and having better social skills in general (Nave, Sherman & Funder, 2008).

With respect to health, higher levels of well-being or happiness are linked to several important outcomes. Although there is extensive research supporting a link between well-being and self-reported health (Lyubomirsky et al., 2005), it is only recently that researchers have been examining the links with more objective, direct evidence of health-related outcomes. For example, one review of over 35 studies found that positive psychological well-being predicts lower subsequent mortality among healthy individuals (Chida & Steptoe, 2008). To the extent that they express positive affect and humour, people with higher levels of well-being may even live longer (Pressman & Cohen, 2007). Well-being can be especially beneficial for those who are already at risk for disease. People with high levels of well-being generally show better prognosis for their health conditions than do people who are anxious or depressed (Pressman & Cohen, 2005; Strine et al., 2008). Psychological well-being also predicts lower mortality for patients with HIV/AIDS and renal failure (Chida & Steptoe, 2008). In one recent study, higher levels of well-being reversed the usual negative effects of low education levels on markers of inflammatory processes (Adler & Rehkopf, 2008), such that low education was associated with less risk for inflammation, but only among those with higher levels of psychological well-being (Ryff, 2010). This finding is especially important given the known links between inflammation and a variety of chronic health conditions including osteoporosis, arthritis, cardiovascular disease and Alzheimer's disease (Ershler & Keller, 2000), and the expected rise in prevalence of these diseases with the greying of the nation in the coming years.

At first it may appear that the links between well-being and favourable life outcomes are somewhat circular, in that the outcomes linked to well-being could easily be viewed as the precursors of well-being. Consider though that the review of the literature by Lyubomirsky and colleagues (2005) not only found correlational associations between well-being and potential outcomes from cross-sectional studies, but they also reported the same findings for longitudinal studies where well-being at Time 1 was linked to outcomes at Time 2, and for experimental studies where well-being was shown to have positive effects on a variety of outcomes under controlled conditions (Lyubomirsky et al., 2005).

Understanding how to enhance and sustain psychological well-being can have some very valuable consequences. It may increase work productivity, as well as enhance financial security for individuals and their families. It can enhance relationship functioning and marital stability for those inclined to find a life partner. Maximizing well-being on the individual level can also have benefits at the community level by increasing community engagement via increased volunteering activity. With respect to health, psychological well-being may serve as a protective buffer against the situational health risks for chronic disease conferred by having a lower level of education, and even increase longevity among both currently healthy individuals and patients with existing health conditions. Given the aging population and the expected increasing demands on the health-care system in the coming years, helping people live healthier, happier lives by increasing and supporting their well-being will be valuable both practically and on the level of quality of life. Although these are just some of the many benefits of well-being that researchers have uncovered to date, clearly they are important and suggest that a better understanding of the ways to increase well-being is a worthy pursuit for both individuals and their communities.

Psychological Health and Well-being research and the people and communities of the Eastern Townships

In this next section I will review some of the key research themes centered on well-being that have been identified by the Psychological Health and Well-being Research Cluster at Bishop's University. I will then briefly discuss their relevance for the people and communities of the Eastern Townships.

The research themes of the Psychological Health and Well-being cluster focus on understanding and enhancing health and well-being across a variety of diverse settings and issues. Six core themes have been identified which form the basis of the corresponding cluster research groups: 1) Self-perceptions, self-regulation, health, and well-being, 2) Chronic illness and pain management, 3) Occupational well-being, 4) Use of health services, 5) Stress, health, and well-being, and 6) Promoting well-being. Table 1 presents these themes along with the sub-themes and examples of ongoing and planned research projects from members of the cluster which will be described in greater detail in the following sections.

Self-perceptions, self-regulation, health and well-being. The first theme addresses the role of self-perceptions and self-regulation in health and well-being. Self-perceptions can include transient views of the self, such as how we view ourselves over time, as well as more en-

Research Theme	Sub-themes	Example projects
1. Self-perceptions, self-regulation, health, and well-being	- Personality and health - Self-perceptions over time and well-being	Goal stocktaking strategies and making healthy changes in the Estrie region
2. Chronic illness and pain management	- Music and pain management - Adjustment to chronic health conditions - Music and well-being	The effects of choir participation on well-being
3. Occupational well-being	- Stress in the workplace and well-being - Violence and aggression in the workplace	Developing better diagnosis, interventions, and policies in occupational mental health: A multi-disciplinary approach Investigating the links between anxiety and professional exhaustion
4. Use of health services	- Health and well-being of Anglophone minority in Quebec - Use of Complementary and Alternative medicine (CAM) - New technology development in the provision of health services	Access to health care in English in the Eastern Townships and its effects on population health laboration et valuation d interventions strat giques cibl es dans le but d am liorer la relation entre les professionnels de la sant et les usagers Anglophones de l Estrie Facilitating Anglophones access to English-language mental health services in the Estrie region
5. Stress, health, and well-being	- Effects of stress on bone health - Coping and resilience	Impact of the economic downturn on psychological health and well-being: A Quebec perspective
6. Promoting well-being	- Motivating health-promoting behaviours - Exercise and well-being - Alternative therapies and well-being, i.e., yoga, meditation, mindfulness	The effects of massage therapy on the executive functioning, physical and psychological well-being of individuals with fibromyalgia

Table 1: Six research themes for the Psychological Health and Well-being Research cluster and sample research projects.

during self-perceptions which are often referred to as personality. How people view themselves impacts not only the goals that they set but also how they approach the sometimes challenging business of trying to reach those goals. For example, seeing oneself as capable of achieving a goal is known to be a powerful motivator for working towards that goal, even in the face of difficult challenges (Bandura, 1986). Accordingly, both transient and more stable self-perceptions necessarily impact the self-regulation of thoughts, behaviours and emotions that are instrumental in the attainment of important personal goals. Indeed, from the perspective of human strengths and flourishing (Park, Peterson & Seligman, 2004), it is important to identify and nurture the characteristics and strategies that promote rather than interfere with adaptive goal regulation. The pursuit and attainment of personally meaningful goals is essential for individual and group survival (Taylor & Pham, 1996), and is associated with a variety of positive outcomes including life satisfaction and enhanced well-being (Martin & Tesser, 1996).

However, it is not only whether or not one is successful in attaining personal goals, but also how one engages in the process of attaining personal goals that has implications for well-being. Pursuing goals relentlessly in a single-minded "the end justifies the means" manner can be maladaptive by making the pursuit of goals joyless and difficult; this can eventually take a toll on health and well-being. The notion that well-being arises from engagement in the process rather than the outcome of goal pursuit is highlighted in the distinction made between telic and autotelic theory. According to Csikszentmihalyi (1982), telic theory locates well-being in the achievement of goals, whereas autotelic theory locates well-being in the movement or flow towards goals. This view is very closely aligned to the eudaimonic perspective of well-being and suggests that shifting the focus from the goal outcome to the goal process may also enhance well-being.

A research project conducted by cluster members that falls under this theme that is active at the time of this writing focuses on the goal strategies that people in the Eastern Townships use when they are trying to make healthy changes. In this project, Claude Charpentier and I examine how people take stock of their goals when they are trying to make healthy lifestyle changes and the implications of these strategies for their health and well-being. Specifically, we are interested in whether strategies that promote engaging in the process of goal pursuit rather than the end result of attaining goals can have beneficial consequences for psychological health and well-being. A secondary aim is to explore the role of self-perceptions or personality in the likelihood of engaging in adaptive goal stocktaking strategies.

Understanding and changing health behaviour is a critical issue that, from a public health perspective, can have significant implications for the health and well-being of people and communities across the life span. The rising rates of obesity and diabetes are directly attributable to poor lifestyle habits that are difficult for many people to change. The results from the research therefore have the potential to assist people who are struggling to reach their health behaviour goals and in this way might improve the health and well-being of people in the Eastern Townships and elsewhere.

Chronic illness and pain management. For individuals diagnosed with a chronic health condition, self-regulation is especially important for disease management and healthy psychological adjustment so as to help maximize their quality of life. Similarly, pain management is critical for those living with chronic conditions in which pain is a central feature. Laura Mitchell, one of the newest cluster members and a new faculty member at Bishop's University in the Department of Psychology, conducts research focused on novel approaches to pain management. Part of her research program focuses on the use of music to manage pain. Although a full detailing of the findings from this innovative research program is beyond the scope of this paper, one of the more interesting findings is counterintuitive to what might be expected with respect to the type of music that is most effective for reducing pain. Rather than classical, jazz or new age music, or any other particular genre of music, Mitchell's research has revealed that it is the listener's preferred music that has the best pain-relieving qualities (Mitchell, MacDonald, Knussen & Serpell, 2007).

In addition to continuing this line of research, Mitchell plans to investigate other ways in which music can enhance well-being. One planned project will examine the potentially beneficial effects of participating in choir for psychological health and well-being, focusing on none other than the members of the Bishop's University Singers.

Occupational well-being. Understanding and enhancing occupational well-being is an important topic of research that several cluster members have begun to address. A large proportion of our daily lives can be spent working; thus, whether or not one is satisfied with one's job or career can impact overall well-being (e.g., Harvey, Kelloway & Duncan-Leiper, 2003). Maximizing work-related or occupational well-being can therefore contribute to improved general psychological health and well-being.

A team of researchers, including cluster member and co-founder Steve Harvey from the Williams School of Business at Bishop's University, is currently examining ways of improving the detection of occupational mental health issues and developing interventions and

policies for dealing with these issues to improve occupational well-being. Similarly, cluster member and co-founder Benoit Bacon and researchers from the Université de Sherbrooke are examining the role of anxiety in professional exhaustion, also known as "burnout". These are just two examples of ongoing projects that aim to improve our understanding of the factors and interventions that may help improve psychological health and well-being in the workplace for people in the Eastern Townships.

Use of health services. This research theme addresses several issues related to the use of both physical and mental health-care services that are of particular importance for Quebec's Eastern Townships given its large number of English-speaking community members. For example, access to health services in English is a key priority for English-speaking Townshippers when they are seeking care for a mental or physical illness (Pocock & Hartwell, 2010). However, not receiving care in one's first language can further complicate existing mental and physical health issues by generating unnecessary stress and because proper care may be foregone (Charpentier, Stout, Benoit, Poulin & Philip, 2011).

Taking a public health promotion approach (Frankish et al., 1996), several cluster members have undertaken research projects to address the issue of accessibility to health-care for the Eastern Township's English-speaking minority. Cluster members Claude Charpentier and Dale Stout from the Department of Psychology are involved in several ongoing research projects which spearhead efforts to address this important issue. One project aims to facilitate better access to needed health-care services in English for the English-speaking community in the Estrie region. Two other related projects headed by cluster member Estelle Chamoux from the Biology Department aim to examine the effects of the availability of health-care access in English on the health and well-being of the English-speaking minority in the Eastern Townships, and further to develop and evaluate interventions to improve the linguistic relationships between health-care providers and the English-speaking patients they treat. This team project involves a number of other cluster members including myself, Claude Charpentier, Dale Stout, Benoit Bacon and Steve Harvey.

Stress, health, and well-being. The deleterious effects of stress on both mental and physical health and well-being are well-established (Elzinga et al., 2008; László et al., 2010; Spruill, 2010), as is the role of individual differences in either amplifying or attenuating these effects (Charles, Gatz, Kato & Pedersen, 2008; Rasmussen, Wrosch, Scheier & Carver, 2006; Sirois, 2007; Sirois, Monforton & Simpson, 2010; Sirois & Tosti, in press). Research that improves our understanding of the

factors that may help ameliorate stress and interventions that can help reduce stress are therefore of utmost importance for enhancing well-being. One ongoing project that I am currently conducting and that reflects the mandates of this theme involves examining the impact of the recession on the health and well-being of Quebec residents over time. In addition to understanding the extent to which the recession has affected people's lives, this study investigates the coping strategies and personality factors that may help buffer the harmful effects of recession-related stress on psychological health and well-being. Because the survey will be administered in both English and French, it will also be possible to examine how French- and English-speaking Quebecers may differ with respect to the impact of the recession and to the factors that promote resilience. These results in particular may provide some insight into how English-speaking people in the Eastern Townships have fared during these economically challenging times.

Promoting well-being. The focus of this final theme is on developing and applying interventions for improving well-being for those who may be at risk for poor well-being, as well as the activities that can promote and maintain well-being in a more pre-emptive manner. One planned project addresses the sub-theme of using alternative therapies for promoting health and well-being among people at risk for poor quality of life. Working with a local massage therapist and with cluster member Andrea Drumheller from Bishop's University's Department of Psychology, I hope to soon launch a study examining the effects of massage therapy for improving the psychological and physical health and well-being of people with fibromyalgia in the Eastern Townships. In addition to pain, sleeping difficulties and cognitive problems including memory issues and decision-making problems (i.e., "fibro fog") are a common debilitating issue in up to 70% of patients (Katz, Heard, Mills & Leavitt, 2004) that can affect their overall quality of life (Miró et al., 2011). This study will examine the effects of 8 weeks of massage therapy on the cognitive functioning of fibromyalgia patients and the associated benefits of this course of therapy for their physical and psychological well-being.

Conclusions

Psychological health and well-being is an important topic with important implications for functioning across a variety of life domains. Rather than simply being an outcome of having one's goals and dreams satisfied, it can enhance outcomes in work life, social and community life, close personal relationships, and even physical health. The recently formed Psychological Health and Well-being research cluster at Bishop's University endeavours to study the ways to better understand

and improve the psychological health and well-being of people in the Eastern Townships (and more globally) by focusing their research across six research themes.

Clearly there is room for overlap among the six research themes outlined. Promoting well-being can involve changing self-perceptions or cultivating the unique strengths and characteristics of individuals and communities to cultivate resilience and buffer stress, as well as using music and other alternative interventions to promote well-being among people with ongoing health issues. Improved access to healthcare for linguistic minorities in the Eastern Townships can minimize stress and promote well-being. Finally, addressing occupational stress can help minimize overall stress and improve health and well-being. By taking this multidisciplinary and multi-pronged approach, we hope to generate theoretical and practical knowledge as well as practical and accessible interventions that may help promote and improve the psychological health and well-being of people in the Eastern Townships.

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STRESS ET MALADIES OSSEUSES : DÉVELOPPEMENT D'UN MODÈLE POUR L'ÉTUDE DES IMPACTS DU STRESS SUR LA SANTÉ OSSEUSE DANS LES POPULATIONS À RISQUE

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Résumé
Le stress est un important déterminant de la santé d'une population. La population de l'Estrie, et plus particulièrement sa minorité anglophone, se trouve dans une situation socio-démographique favorisant de hauts taux de stress. Plusieurs systèmes physiologiques sont fortement affectés par les hormones sécrétées lors d'un stress et c'est particulièrement le cas du système ostéo-articulaire. Il est donc probable que de hauts niveaux de stress perturbent l'équilibre du métabolisme osseux et favorisent l'émergence de pathologies ostéo-articulaires telles que l'ostéoporose ou l'arthrite rhumatoïde. Les études sur le sujet sont parfois contradictoires et mal adaptées à l'étude de la situation chez l'être humain. De plus, il n'existe pas de méthode facile pour évaluer l'activité de résorption osseuse chez les individus d'une population. Nous présentons ici un modèle de culture cellulaire permettant de dériver des cellules ostéoclastiques humaines à partir d'une simple prise de sang. Nous montrons également que l'hormone principale sécrétée lors d'un stress, le cortisol, modifie les capacités résorbantes des cellules osseuses. Ces résultats donnent une base solide pour le développement d'une étude populationnelle évaluant l'impact du stress sur la santé osseuse de la population de l'Estrie.

Abstract
Stress is an important determinant of health in a population. People in the Eastern Townships, particularly the English-speaking minority, face a unique socio-demographic situation which may favour high stress levels. Several body systems are affected by stress hormones. This is particularly true for the skeletal system. It is likely that high levels of stress modify the balance of bone metabolism and favour

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bone and joint disorders like osteoporosis or rheumatoid arthritis. Studies on this subject are sometimes contradictory and poorly adapted to the study of the situation in humans. Moreover, no easy method exists to evaluate bone resorbing functions in the individuals of a population. The work reported here presents a model of cell culture generating human osteoclast-like cells from a simple blood sampling. We also show that the main human stress hormone, cortisol, modifies the resorbing capacities of bone cells. These results provide a solid foundation for the future development of a study at the population level, evaluating the impact of stress on bone health in the Eastern Townships.

Introduction

Le stress est l'un des plus importants déterminants de santé établis par Santé Canada[1]. Le rôle du stress sur la santé physique est multiple et complexe, d'autant plus qu'une considérable variabilité individuelle rend les études difficiles à analyser. On peut cependant établir plusieurs liens directs entre stress et santé physique grâce à une meilleure compréhension des effets physiologiques du stress[2]. La phase initiale du stress est caractérisée par une réaction intense et de courte durée au cours de laquelle les glandes médullo-surrénales, activées par le système nerveux central, sécrètent d'importantes quantités de catécholamines (adrénaline et noradrénaline essentiellement) dans le sang[3]. Après quelques minutes, les glandes cortico-surrénales sont activées à leur tour et sécrètent des glucocorticoïdes (principalement le cortisol et la cortisone chez l'Homme) pendant parfois plusieurs heures[3]. Si la situation stressante perdure, la sécrétion de glucocorticoïdes surrénaliens est appelée à durer dans le temps[3]. D'ailleurs, il est bien démontré que les personnes souffrant de dépression majeure ont des taux de cortisol sanguins significativement plus élevés que les personnes en bonne santé mentale[4].

Les effets des glucocorticoïdes sur l'organisme sont de plusieurs ordres et peuvent inclure l'inhibition de la fonction immunitaire, une augmentation de la pression sanguine, la modification du métabolisme et la redistribution des réserves de graisse corporelle ou encore une inhibition de la fonction reproductive[5-7]. L'un des systèmes physiologiques particulièrement touché par les effets délétères des glucocorticoïdes est le squelette[8]. En effet, bien qu'il s'avère souvent nécessaire d'administrer des glucocorticoïdes pour le traitement de maladies auto-immunes ou inflammatoires, les études réalisées sur des patients placés sous corticothérapie démontrent une diminution de la masse osseuse de près de 12% en moins d'un an. Après seulement trois

mois de corticothérapie, le risque de fracture augmente de 75%[9-12] quel que soit le site étudié ou le régime de thérapie utilisé. Cependant, il reste difficile encore aujourd'hui de bien comprendre et prévenir les effets osseux des glucocorticoïdes. En particulier, l'impact de niveaux de glucocorticoïdes élevés dus à une situation stressante chronique reste à évaluer. Plusieurs études démontrent que la dépression[13-16] ou l'hypercorticisme subclinique[17-21] (taux de cortisol élevés) favorisent les problèmes de santé osseuse.

En 2008, une enquête réalisée auprès de la population québécoise montrait que 28% de la population ressentait un niveau de stress élevé[22]. La situation socio-démographique en Estrie est particulière et présente plusieurs spécificités contribuant à élever le niveau de stress ressenti et le risque de détresse psychologique[23-25]. De plus, la population anglophone de l'Estrie est généralement plus âgée, plus isolée et plus défavorisée matériellement que les autres personnes résidant en Estrie[26]. En raison des impacts psychologiques qu'elle peut entraîner, cette situation matérielle et sociale pourrait avoir de sérieux impacts sur la santé osseuse de la population estrienne.

De façon générale, les pathologies ostéo-articulaires sont en augmentation constante dans les pays occidentaux[28], une tendance accrue par le vieillissement des populations. Près de deux millions de Canadiens souffrent d'ostéoporose[28, 29], une pathologie osseuse le plus souvent asymptomatique jusqu'à l'apparition de fractures. Elle affecte majoritairement les femmes de plus de 50 ans[30]. Évalués à 1,9 milliards de dollars chaque année, les coûts engendrés par les traitements de l'ostéoporose ou de ses conséquences pèsent lourdement sur notre système de santé. Plus de la moitié des patients sont incapables de retourner à la maison à la suite d'une fracture de la hanche et sont orientés vers des soins de moyenne ou longue durée[31]. De plus, une vaste étude canadienne multicentrique sur l'ostéoporose (CaMOS) portant sur plus de 10,000 personnes établissait récemment que jusqu'à 70% des fractures de la hanche dues à l'ostéoporose provoquent la mort ou une incapacité permanente[27, 32]. L'ostéoporose représente donc une charge considérable sur les sociétés occidentales. Si un grand nombre de facteurs de risque ont été identifiés, on ne connaît pas de cause particulière à l'ostéoporose et la prévention fait une large part aux habitudes de vie (nutrition, exercice physique...), bien que la gestion du stress soit encore relativement peu prise en compte.

L'effet marqué des glucocorticoïdes sur le squelette est le résultat d'actions directes et indirectes sur le métabolisme osseux: jouant au niveau systémique sur le métabolisme endocrinien (inhibition de la sécrétion de stéroïdes gonadiques) et phosphocalcique (diminution de l'absorption intestinale et rénale du calcium)[33], les glucocorticoïdes

agissent également dans le microenvironnement osseux[34, 35] et au niveau cellulaire. On rapporte un effet fortement inhibiteur sur les ostéoblastes, cellules responsables de la formation osseuse, et une modification des voies de signalisation de l'ostéoclaste, cellules responsables de la résorption osseuse[21, 36-38]. Si les effets inhibiteurs des glucocorticoïdes sur la formation osseuse sont bien documentés, il n'en va pas de même pour leurs effets sur la résorption. Or un squelette en santé dépend essentiellement de ces deux paramètres, soit la formation et la résorption osseuse, qui doivent être maintenues en équilibre tout en assurant un remodelage constant du tissu osseux[39]. Un cycle de remodelage débute par une intense activité des cellules résorbantes (ostéoclastes) menant à la formation d'une lacune de résorption. Une fois la lacune exposée au milieu environnant, sa surface est colonisée par des ostéoblastes qui combleront l'espace avec une matrice osseuse nouvellement synthétisée. Le recrutement et l'activité des ostéoblastes étant avant tout déterminés par l'activité initiale des ostéoclastes, la plupart des stratégies thérapeutiques visent à influencer le niveau de résorption[40, 41].

La plupart des études sur le sujet indiquent que les glucocorticoïdes augmentent la durée de vie des ostéoclastes[36, 42]. Par contre, l'effet des glucocorticoïdes sur l'ostéoclastogénèse et l'activité résorbante des ostéoclastes varient selon le modèle étudié[36, 38, 42-45]. Plusieurs études démontrent qu'une stimulation par les glucocorticoïdes enclenche une modification de l'architecture cellulaire (cytosquelette d'actine) et induit le détachement de l'ostéoclaste de sa matrice osseuse[36, 46]. En conséquence, dans ce modèle les glucocorticoïdes auraient un rôle plutôt inhibiteur sur la résorption osseuse, ce qui apparaît contradictoire avec les observations faites chez les patients humains. Une étude plus récente démontre au contraire que les ostéoclastes humains, stimulés in vitro par des glucocorticoïdes adhèrent plus solidement à la matrice osseuse et arrêtent de se déplacer à la surface de l'os[47]. Il en résulte des lacunes de résorption qui, au lieu d'être allongées et de faible profondeur, ont plutôt une allure de puits restreints en surface mais de plus grande profondeur. Ceci pourrait contribuer à fragiliser la structure de l'os en profondeur, d'autant plus que la partie résorbée est moins accessible aux ostéoblastes chargés de reformer la nouvelle matrice osseuse. Ces études sont cependant sporadiques et ne décrivent pas toujours les mécanismes cellulaires et moléculaires mis en jeu. Il n'existe pas de lignée cellulaire d'ostéoclastes humains et les modèles de rongeurs sont inadaptés. Prenant exemple sur un modèle bien établi à partir de cellules du sang de cordon ombilical[48-51], nous avons développé et raffiné un modèle d'ostéoclastes humains capables de résorber l'os in vitro, à partir de cellules du sang périphérique. Il s'agit d'un

modèle de cultures primaires requérant temps et expertise, mais qui permet de faire face au défi le plus important pour ce genre d'études : **obtenir des cellules d'origine humaine ayant un fonctionnement se rapprochant des activités cellulaires *in vivo***. L'article présenté ici est une description du modèle d'étude suivie d'une analyse de l'action des glucocorticoïdes sur les interactions entre la cellule ostéoclastique humaine et la surface osseuse.

Matériels et méthodes

Modèle cellulaire d'ostéoclastes humains

Le modèle d'ostéoclastes humain est dérivé de monocytes du sang périphérique de donneurs volontaires recrutés dans la région de l'Estrie. Après avoir reçu toute l'information nécessaire, 27 femmes pré-ménopausées ont signé le formulaire de consentement et ont intégré notre protocole de recherche (approuvé par le comité d'éthique de l'Université Bishop's). En bref, 50 ml de sang périphérique ont été prélevés par prise de sang au pli du coude. Les leucocytes ont été isolés du sang par centrifugation (20 min, 2000 rpm) sur Ficoll-Paque (GE Healthcare), puis ensemencés sur une surface de verre traitée à une densité de 3 millions/ml et dans un milieu sélectif (OPTI-MEM supplémenté de 100pg/ml de GM-CSF[i]) pendant 24 heures. Les cellules non-adhérentes, correspondant en majorité aux lymphocytes et neutrophiles, ont été retirées après 24 heures en même temps que le milieu sélectif. Seules les cellules adhérentes, constituées en majorité de monocytes, restaient alors dans la culture. Un milieu de différenciation contenant du M-CSF[ii] (25 ng/ml) et du RANKL[iii] (100 ng/ml) a ensuite été ajouté et changé tous les 2 à 3 jours. Après quatre semaines, les cellules multinucléées générées ainsi expriment les marqueurs typiques des ostéoclastes (Calcitonine, V-ATPase, activité Phosphatase Acide Résistante au Tartrate) et sont capables de résorber l'os, tout comme cela avait été démontré pour les ostéoclastes dérivés de monocytes ombilicaux[49, 51, 52]. Au cours des deux dernières semaines de culture, des doses de cortisol humain variant de 10^{-11} à 10^{-5} M ont été ajoutées aux milieux de culture à chaque changement de milieu. Chaque dose de cortisol a été testée sur au moins 3 échantillons de cellules par donneuse.

Immunocytochimie Afin de vérifier l'expression de marqueurs indiquant la présence de cellules ostéoclastiques, les cellules ont été fixées à la fin de la période de culture à l'aide d'une solution de paraformaldéhyde 1% dans un tampon phosphate. Après plusieurs lavages, les sites non-spécifiques ont été bloqués avec une solution de

[i] GM-CSF : Granulocyte Macrophage-Colony Stimulating Factor
[ii] M-CSF : Monocyte-Colony Stimulating Factor
[iii] RANKL : Receptor Activator of NF-kB Ligand

lait écrémé 5% et les peroxydases endogènes saturées à l'aide d'une solution contenant 3% de peroxyde d'hydrogène. Des anticorps primaires dirigés contre le récepteur à la calcitonine (Santa Cruz Biotechnologies, utilisé 1:50) ou contre la pompe V-ATPase (BD biosciences, utilisé 1:50) ont été utilisés comme marqueurs[51]. Après une incubation d'une heure à 37°C, les cellules ont été lavées pour ôter l'excédent d'anticorps primaires puis recouvertes d'une solution contenant un anticorps secondaire universel couplé à la streptavidine (Dako Cytomation). Après 45 minutes d'incubation, l'excédent a été lavé puis une solution de biotine couplée à la peroxydase de raifort (Dako Cytomation) a été appliquée sur la culture de cellules durant 30 minutes. Après le retrait de l'excédent, un substrat incolore a été ajouté. Les sites contenant de la peroxydase ont pris une teinte rouge/brunâtre en raison de l'oxydation du substrat incolore. Un contre-marquage des noyaux a été réalisé à l'aide d'hématoxyline afin de concentrer l'analyse sur les cellules comportant plus de 3 noyaux.

Résorption osseuse

Le même protocole d'isolement et de culture cellulaire a été réalisé en présence d'une lamelle osseuse placée au fond du puits de culture. Les lamelles osseuses de 150 mm d'épaisseur ont été tranchées au laboratoire à partir d'os bovins obtenus dans le commerce. À la fin de la période de culture, les lamelles osseuses ont été retirées des puits et passées dans une solution contenant 1% de NaOH puis soniquées durant 1 minute afin de retirer les cellules de la surface osseuse[51]. Ensuite, les lamelles ont été immergées dans une solution de bleu de toluidine 1% durant 1 minute. Après rinçage à l'eau courante, la surface érodée correspondant aux lacunes de résorption laissées par les ostéoclastes apparaissait en bleu/violet.

Anneaux de résorption

À la fin de la période de culture, les ostéoclastes ont été fixés à l'aide d'une solution contenant 1% de paraformaldéhyde. Une solution de triton-100 1% a été appliquée durant 10 minutes afin de perméabiliser les membranes cellulaires, puis les sites non-spécifiques ont été bloqués grâce à une solution contenant 5% de lait écrémé. Une solution contenant de la Phalloïdine-Alexa633 (Invitrogen, utilisée 1:200) a été appliquée sur la culture cellulaire pendant une heure. Après lavage de l'excédent, un contre-marquage des noyaux a été effectué à l'aide d'une solution contenant du DAPI afin de visualiser les cellules multinucléées. Les lames ont ensuite été visualisées à l'aide d'un microscope confocal Olympus et prises en photo à l'aide d'une caméra numérique et du logiciel Fluoview.

Résultats & Discussion

Nous souhaitions pouvoir obtenir des ostéoclastes facilement, provenant d'individus de la population générale et en utilisant une procédure faiblement invasive. Un modèle d'ostéoclastes humains avait été développé il y a plusieurs années à partir de sang de cordon ombilical[49, 51, 52] : bien que très utile pour un grand nombre de recherches, il nous fallait modifier ce modèle de cellules fœtales afin de pouvoir étudier la physiologie des ostéoclastes provenant d'hommes ou de femmes adultes à différents stades de leur vie. Après avoir adapté et raffiné le protocole, nous avons isolé des cellules ayant les caractéristiques d'ostéoclastes matures capables de résorber l'os à partir du sang périphérique d'individus adultes. Dans le but de réaliser dans le futur des études populationnelles, il était important de valider ce modèle permettant d'obtenir des cellules ostéoclastiques humaines à partir d'une simple prise de sang. Comme le montre la Figure 1, les cellules générées par cette technique de culture sont multinucléées et expriment l'intégrine VLA-2 (récepteur du collagène) ainsi que la pompe V-ATPase. La pompe V-ATPase est une pompe nécessaire au recaptage actif des protons sécrétés dans la lacune de résorption et servant à dissoudre la matrice osseuse minérale[53, 54]. Localisée dans la bordure en brosse au contact de la matrice osseuse, la présence de cette pompe est fortement indicative d'ostéoclastes actifs (Figures 1A et D). L'intégrine VLA-2 n'est pas spécifique aux ostéoclastes puisqu'elle est retrouvée dans une vaste proportion de cellules. Cependant, ce récepteur du collagène est fortement exprimé dans la zone scellée entourant la lacune de résorption, indiquant alors la présence d'un ostéoclaste mature et bien adhéré à sa matrice (Fig. 1B et D). La présence de ces deux marqueurs localisés respectivement au niveau de la lacune de résorption et dans la zone scellée délimitant cette dernière nous indique que le processus de maturation de ces cellules est complet.

Parallèlement à ces marqueurs, nos analyses montrent la présence de lacunes de résorption à la surface des lamelles osseuses sur lesquelles les cellules ont été cultivées (Figure 2). Ceci indique que notre modèle de culture génère, à partir du sang périphérique de donneurs, des cellules exprimant les principales caractéristiques d'ostéoclastes matures et actifs. Nous travaillons en ce moment à l'étude des gènes exprimés dans ces cellules afin de parfaire la validation de notre modèle. Il doit nous permettre à l'avenir de déterminer si le cortisol influence la maturation et l'activation des ostéoclastes. En perspective, ce modèle nous permettra également de mesurer l'impact du stress ressenti sur l'ostéoclastogénèse.

Afin de déterminer l'effet du cortisol sur l'établissement d'un site de résorption caractérisé par l'apparition d'un anneau d'actine, des

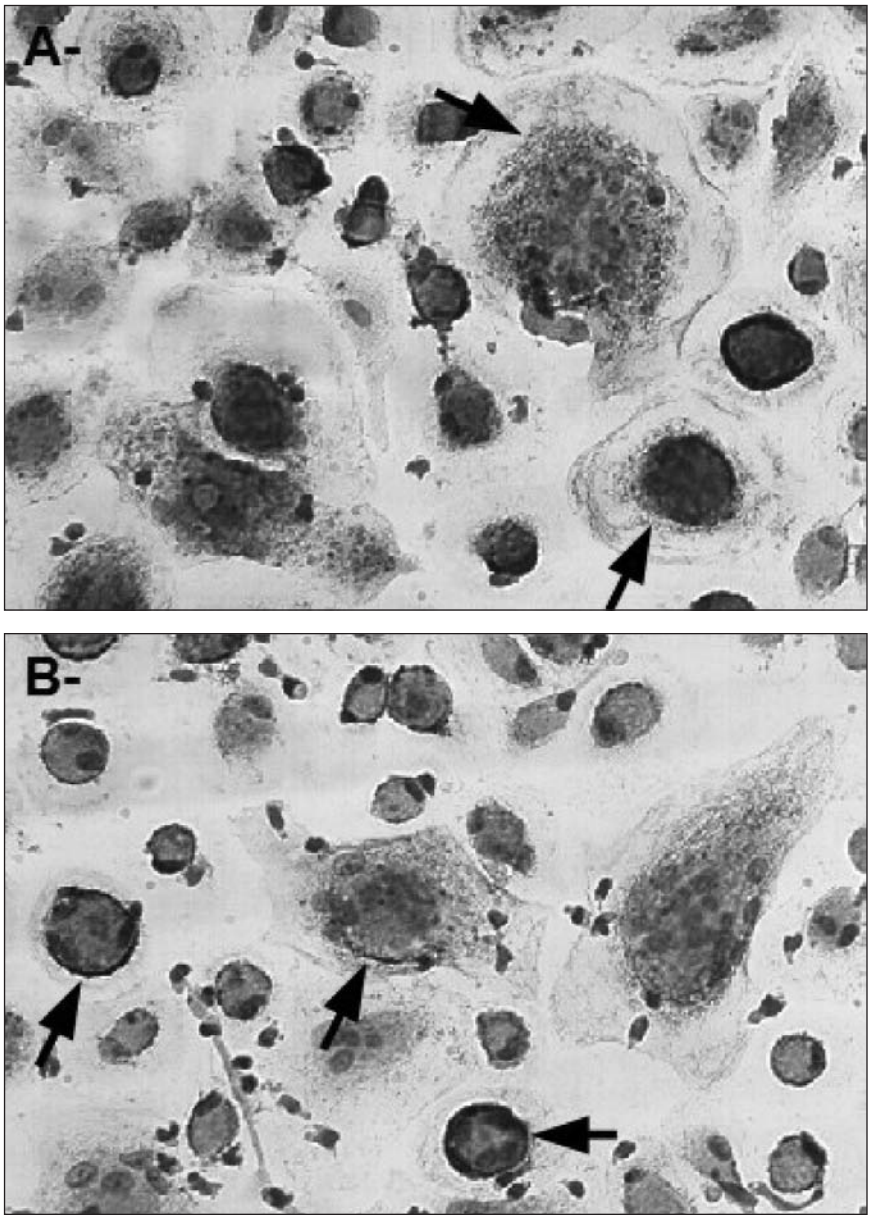
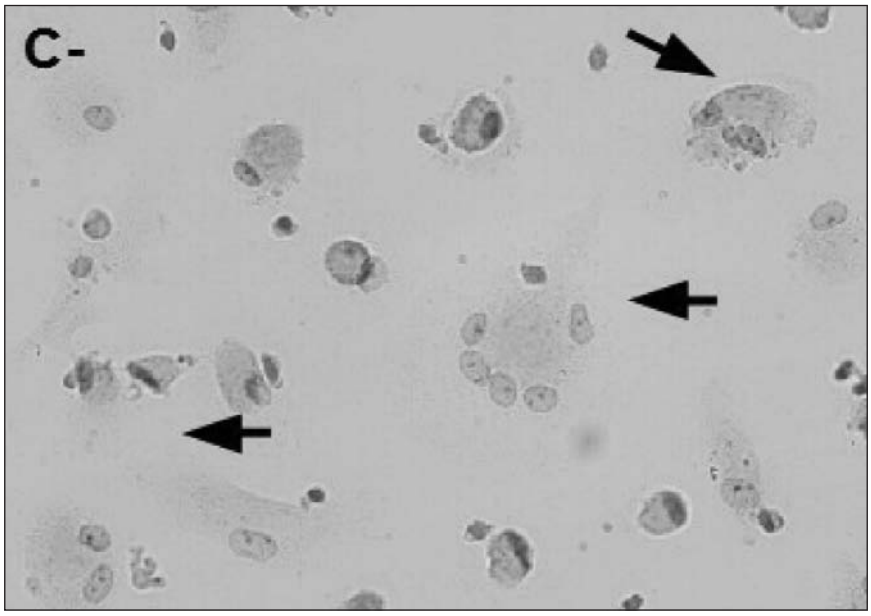
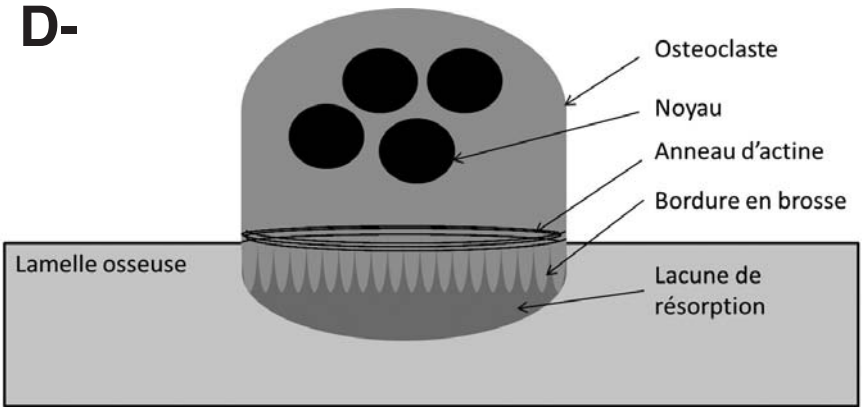


Figure 1 : Expression des marqueurs ostéoclastiques à la surface membranaire. Après culture, l'expression de marqueurs caractéristiques d'ostéoclastes matures a été analysée. A) Expression de la pompe V-ATPase, exprimée dans la bordure en brosse au contact de la lacune de résorption. La coloration brun-rouge représente les zones où cette pompe est exprimée, soit à l'intérieur de la zone scellée délimitant la lacune de résorption (flèches). B) Expression de l'intégrine VLA-2, récepteur du





collagène. L'expression de ce marqueur est retrouvée au niveau de la zone scellée, zone d'adhésion la plus forte de l'ostéoclaste à sa matrice (flèches). C) Marquage non-spécifique : sur cette lamelle, seul l'anticorps secondaire a été utilisé. On distingue bien les ostéoclastes par leur nombre de noyaux, marqués à l'hématoxyline, mais aucun marquage brun-rouge n'est présent attestant la spécificité des marqueurs utilisés. D) Schéma représentant un ostéoclaste résorbant la surface osseuse sur laquelle il est fixé.

cultivées en présence de doses croissantes de cortisol (Figures 3 B, C, soit 10^{-11} M, 10^{-10} M et 10^{-9} M respectivement, correspondant à la normale des taux circulants). Les doses de 10^{-7} à 10^{-6} M, correspondant à des taux élevés de cortisol sanguin, augmentent de façon notable le nombre et l'intensité des anneaux d'actine observés. Cette observation suggère que des niveaux de stress élevés pourraient favoriser l'établissement de sites de résorption. Bien que les mécanismes cellulaires mis en jeu n'aient pas encore été disséqués dans notre modèle, l'analyse d'autres études nous indique des pistes pour expliquer le rôle du cortisol sur l'adhésion de l'ostéoclaste à sa matrice osseuse : l'anneau d'actine est une structure constituée de protéines filamentaires organisées à la manière d'un squelette microscopique. Localisé à la jonction entre la membrane cellulaire et la surface osseuse, l'anneau d'actine est crucial pour maintenir l'adhésion et l'activité résorbante de l'ostéoclaste[55].

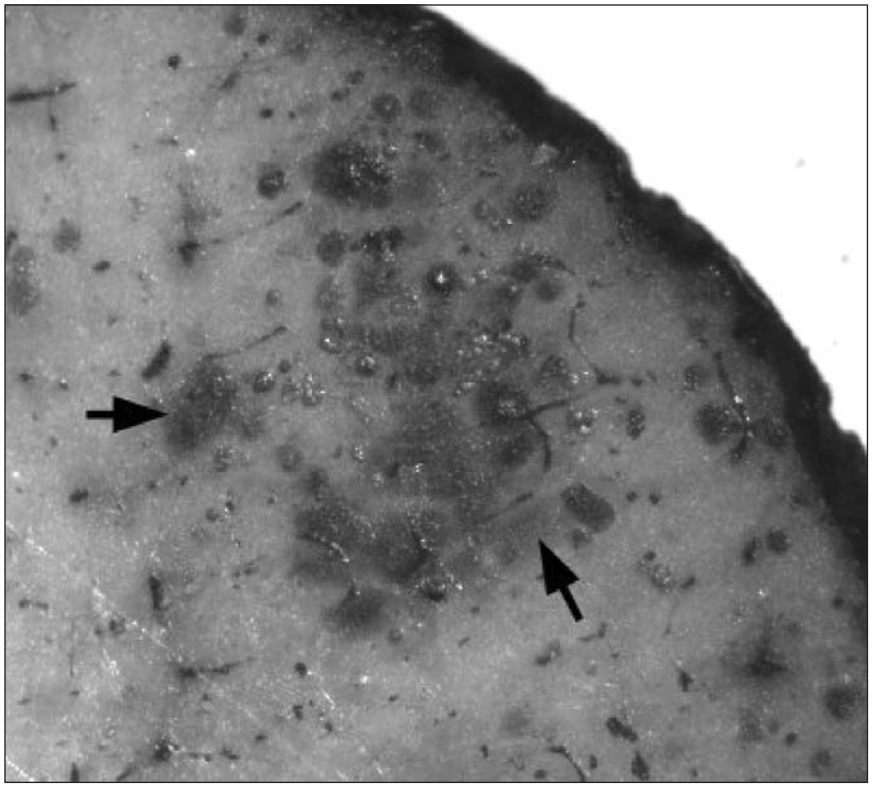


Figure 2 : Lacunes de résorption visualisées sur une lamelle osseuse. Après induction de la différenciation et de la maturation des cellules cultivées sur lamelles osseuses, les cellules ont été retirées et les lamelles osseuses colorées au bleu de toluidine. La lacune de résorption, dont la surface est érodée, fixe le colorant plus fortement que l'os non résorbé (flèches).

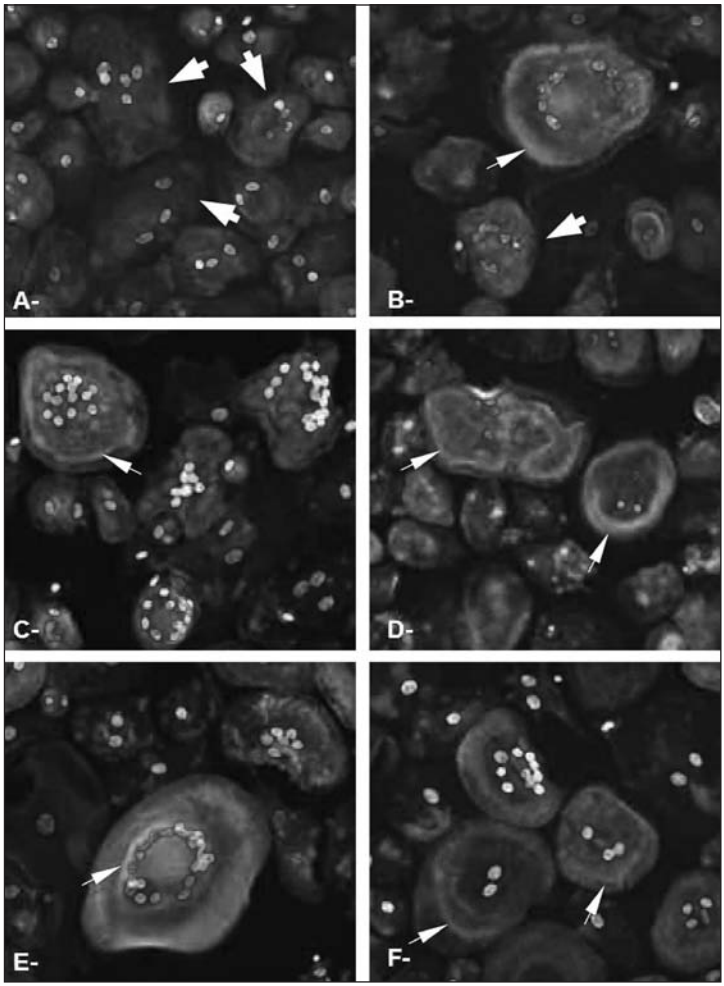


Figure 3 : Formation d'anneaux d'actine délimitant la zone scellée. Les cellules ont été cultivées pendant les deux dernières semaines de leur maturation en présence de doses croissantes de cortisol. L'un des échantillons n'a pas été traité au cortisol afin de servir de contrôle. Nous avons utilisé des doses de 10^{-11}M à 10^{-5}M afin de couvrir les taux physiologiques (<10^{-9}M) ainsi que les taux thérapeutiques ou pathologiques (>10^{-7}M). Toutes les photographies ont été prises à l'objectif 40X. A) Cellules non-traitées au cortisol. Les ostéoclastes multinucléés se distinguent clairement (grosses flèches), mais peu de cellules exposent un anneau d'actine bien délimité. B) À des doses aussi faibles que 10^{-11}M, un marquage plus dense de l'actine est observé dans la région de la zone scellée (petite flèche). C, D, E, F) Doses de 10^{-10}, 10^{-9}, 10^{-7} et 10^{-6}M respectivement: de plus en plus de cellules présentent un anneau d'actine bien marqué et franchement délimité (petites flèches). La proportion de cellules présentant ces anneaux d'actine semble augmenter avec la dose de cortisol utilisée.

Cet anneau d'actine demeure malgré tout extrêmement dynamique et se réorganise constamment afin de maintenir l'adhésion ou au contraire favoriser le détachement de l'ostéoclaste, en fonction des besoins et des stimuli hormonaux[56, 36, 46]. Selon les mêmes études, toutes réalisées chez les rongeurs, les glucocorticoïdes induisent la dissolution de l'anneau d'actine et provoquent le détachement des ostéoclastes de la matrice osseuse. Nos résultats suggèrent au contraire que les cellules ostéoclastiques humaines sont plus fortement adhérentes à la surface osseuse lorsque du cortisol est présent dans le milieu de culture, ceci même à des doses physiologiques. Nos résultats correspondent à ceux d'une autre étude récente démontrant que les ostéoclastes humains mis en présence de glucocorticoïdes génèrent des lacunes de résorption plus profondes et moins étendues[47]. En effet, plus l'anneau d'actine est marqué, moins l'ostéoclaste est susceptible de se détacher et de se déplacer à la surface de l'os[57]. Afin de valider cette hypothèse, des études seront menées à l'aide d'enregistrements vidéo et le suivi de la migration des ostéoclastes à la surface osseuse sera analysé par des algorithmes de migration établis précédemment pour d'autres études.

Les résultats présentés ici sont encore préliminaires. Nous cherchions à valider un modèle d'étude nous permettant de réaliser des études populationnelles afin de déterminer si le niveau de stress subi au quotidien influence le niveau de résorption osseuse et, par là-même, le risque de déséquilibre entre résorption et formation osseuse. Cependant, nos résultats permettent d'élaborer une hypothèse de travail selon laquelle le cortisol favoriserait l'adhésion des ostéoclastes à la matrice osseuse et ainsi l'augmentation des sites de résorption. Notre modèle nous permettra dans l'avenir de tester cette hypothèse et éventuellement d'apporter des arguments physiologiques en faveur d'une prise en charge du stress pour la prévention et le traitement des maladies osseuses. Plusieurs études pointent la dépression, favorisée par le stress, comme un facteur de risque pour l'ostéoporose[14-16, 58]. Il est également bien documenté que les patients souffrant d'arthrite rhumatoïde voient l'intensité de leurs symptômes suivre un rythme circadien proche de celui du cortisol[59, 60]. Les taux de cortisol sont plus élevés chez les patients arthritiques que chez les sujets sains, mais on constate surtout que le rythme de sécrétion est modifié chez ceux ayant des atteintes sévères[61]. Il est également clairement montré que les stress mineurs de la vie quotidienne affectent négativement le pronostic à long terme des patients arthritiques[62, 63]. Plus encore, le développement de l'arthrite juvénile est souvent précédé d'un événement stressant majeur, peu de temps avant l'apparition des symptômes[64]. De plus en plus de données permettent aujourd'hui de

considérer le stress comme un facteur prédisposant et aggravant pour les maladies ostéo-articulaires, qu'elles soient de nature inflammatoire ou métabolique.

Un grand nombre de facteurs influencent également l'exposition de l'organisme aux glucocorticoïdes[4, 65]. Plusieurs facteurs sont d'importants vecteurs de stress dans la vie de tous les jours, notamment le statut socio-économique, l'isolement et les problèmes de santé[66, 67], des problématiques touchant plus particulièrement la minorité anglophone de l'Estrie[68]. Il est donc primordial de s'interroger sur les niveaux de stress, sur l'état de santé psychologique et des effets de ces derniers sur la santé générale de la population estrienne. La validation de notre modèle, présenté ici, nous permettra de réaliser une étude visant à déterminer les impacts de cette situation particulière sur la santé osseuse de la population de l'Estrie.

À plus long terme, les données obtenues devraient nous permettre de mieux comprendre les effets du bien-être psychologique sur le métabolisme osseux et de déterminer si de forts niveaux de stress constituent un facteur prédisposant et/ou aggravant pour les pathologies ostéo-articulaires. Si tel est le cas, nos conclusions pourraient ouvrir la voie à de nouvelles interventions de santé publique, plaçant le bien-être psychologique au cœur des stratégies de prévention des maladies osseuses, ceci dès l'atteinte du pic de masse osseuse. Les campagnes à l'heure actuelle mettent l'accent sur la nutrition et l'exercice physique. Promouvoir le bien-être psychologique pourrait constituer un autre angle d'attaque des campagnes de prévention ou au cours des traitements de réhabilitation.

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