Does Envy Induce Bone Loss Like Depression and Stress?

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While significant elevation of the glucocorticoid cortisol has been linked to bone loss in depression and stress and it can be elevated by negative emotions, short term elevations as may occur in episodic envy are unlikely to measurably impact bone density. The difficulty in securing an adequate research sample of subjects demonstrating chronic, debilitating envy makes research in this regard challenging, but available evidence points to intriguing clues about its potential effects on human health.

Recently a mechanism for the induction of bone loss as a function of chronic envy was proposed (Sabol, 2017) based in significant measure on a model of inhibitory control and avoidance learning proposed by Vadovicova and Gasparotti (2014) where the dorsal anterior cingulate cortex (dACC) generates a warning about the harmful consequences of behavior. With its reciprocal connections with the anterior insula (IA) and association with basal ganglia, this adversity processing circuit, which includes direct projections from dACC, projects to the lateral habenula (LHb) which in turn inhibits release of serotonin and dopamine in the brainstem and midbrain. The co-activation of all three areas - dACC, AI and LHb – was supported by functional magnetic resonance imaging (fMRI).

Brain derived serotonin appears particularly significant to bone health since it regulates bone mass accrual through a biochemical signaling cascade in ventromedial hypothalamus (VMH) neurons (Oury et. al., 2010). Serotonin binds to a receptor – Htr2c – expressed in the VMH neurons, ultimately resulting in the inhibition of epinephrine synthesis and thereby decreasing sympathetic tone. This decrease is relayed to osteoblasts, decreasing resorption and increasing bone formation (Ducy, et. al., 2010). So the adversity processing circuit may inhibit serotonin release from the dorsal raphe nucleus (DRN) as a result of the risky and destructive behaviors we may associate with chronic, debilitating envy, especially since dACC has been shown to be activated by fMRI when people feel envious (Takahashi et. al., 2009). Interestingly, the DRN has been linked to bone loss in a tau model of Alzheimer's disease (Dengler-Crish, Smith and Wilson, 2017).

When investigating alternative mechanisms shaping the role negative emotions like envy may play in skeletal health it is instructive to note physiological systems which impact bone metabolism. Mezuk and Golden (2009) noted that depression is associated with alterations in four such mechanisms: inflammation, including the production of cytokines, hypothalamic – pituitary – adrenal (HPA) axis activation with resultant hypercortisolism, sympathetic nervous system activation and hypogonadalism. Azuma et. al. (2015), in discussing chronic psychological stress as a risk factor for osteoporosis, delineate

exactly these factors (while adding suppression of growth hormone secretion) in noting that chronic mental stress activates the SNS into inducing higher glucocorticoid and catecholamine release, leading to bone loss. Wippert et. al. (2017) also invoke the HPA axis and its effects on altered release of growth hormones, glucocorticoids and cytokines in finding "compelling evidence" that biochemical and psychoneuroendocrinological maladaptations caused by mental stress are relevant to bone quality. Glucocorticoids, stress hormones that include cortisol, block assimilation of calcium in the intestines and excessive secretion of them as seen in chronic stress can cause urinary calcium loss, increase bone resorption and inhibit bone growth. They are a risk factor for bone health in patients receiving massive doses for disease conditions as well as in Cushing's syndrome, where cortisol is hypersecreted.

There is evidence for stress hormonal activity associated with depression playing a role in the induction of bone loss (Yirmiya et. al., 2006). Also, subordinate (nondominate) female cynomolgus macaques subjected to social stressors had lower bone density and higher morning cortisol concentrations than their dominant counterparts in addition to other physiological consequences, including suboptimal serotonergic and dopaminergic functioning (Shively and Day, 2014). Additionally, mice exposed to overcrowded cages for three weeks showed significant bone demineralization (Burkovskaya, Frontasyeva and Gundorina, 1994).

However, short term elevations in cortisol as may occur in episodic envy are unlikely to meaningfully impact bone density (Liponis, 2017), although there is statistical evidence for the correlation of envy with both depression (Sabol, 2017) and stress: Thompson, Glaso and Martinsen (2016), using questionnaires constructed by Kidwell, Jr. and Robie (2003), found envy positively correlated with distress, rs (Spearman's rho) = .44, p = .01, and also B (standardized beta) = .55, p = .001. Further, dispositional envy has been linked to anxiety as well as hostility, a hallmark of envy which is a strong predictor of cardiovascular disease, higher systolic blood pressure and elevations in cortisol; anger has been associated with envy and has also been linked to HPA activation (Pila, 2011). The emotional and physical arousal induced by negative emotions acting in conjunction arguably puts individuals manifesting chronic, debilitating envy (CDE) at risk for the negative outcomes associated with them, such as the bone loss induced by depression and stress described above.

It may be that all we can conclude at present is that envy, like depression and stress, is a distinct factor that may contribute as one negative emotion among several to activation of the HPA axis and all that implies for bone health. A difficulty here is securing an adequate research sample manifesting CDE; there is no such DSM-5 diagnosis but neuroscience has yielded some intriguing results, at least in respect to dispositional envy as assessed by the Dispositional Envy Scale (Smith et. al., 1999). While the laboratory research described above associated episodic envy with the dACC via fMRI, this instrument has also been used to examine neural correlates of envy. The difference is roughly of that between acute and chronic envy. In one interesting report, Xiang et. al. (2017) found that one area where it positively correlated with gray matter volume (GMV) using voxel-based morphometry (VBM) was the superior temporal gyrus (STG). Loskutova et. al. (2010), using MRI, x-ray absorptiometry and VBM found low bone mineral density (BMD) associated with low GMV in the left STG and other areas in early

Alzheimer's disease patients, suggesting that in these subjects the central mechanisms of bone remodeling is disrupted by neurodegeneration. However, results were negative for their non-demented controls, and lowered BMD and osteoporosis correlate more significantly with Alzheimer's patients than with normal controls (Bednarski et. al., 2014).

Further investigation may ultimately demonstrate a compelling causal relationship between envy and bone loss. Meanwhile, the activation of the dACC during episodic envy and the key role it may play as part of an adversity processing circuit that inhibits serotonin release should continue to make it an intriguing possibility as part of such a mechanism.

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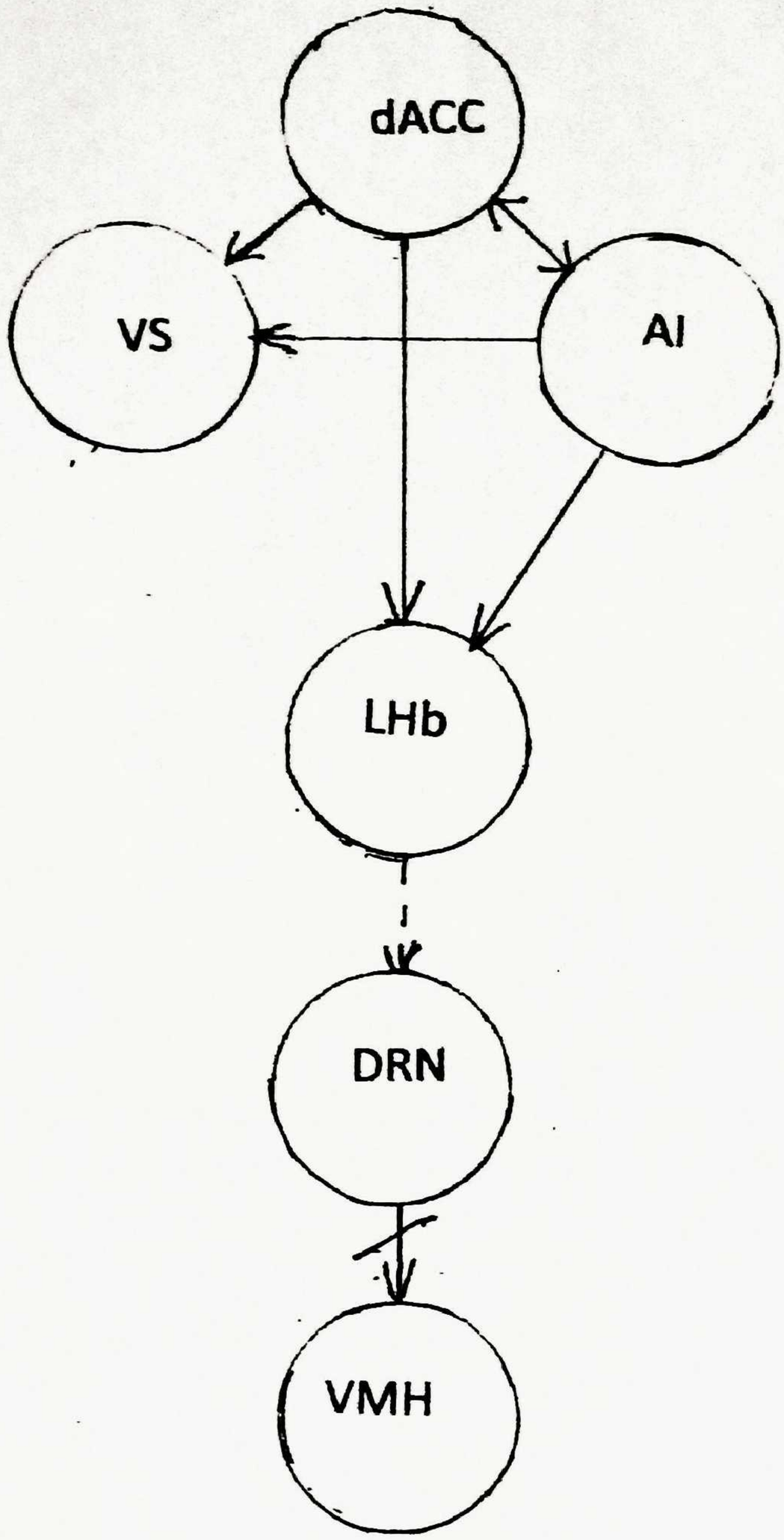
ADDENDUM



Top portion is a simplified representation of the Vadovicovian adversity processing circuit, including the dorsal anterior cingulate cortex (dACC), which is activated during envy and signals this system to act. AI is anterior insula, VS is ventral striatum with D2 dopamine receptors, LHb is lateral habenula, from which inhibitory projections (represented by broken lines) inhibit serotonin release from the dorsal raphe nucleus (DRN).

Serotonin binds to the Htr2c receptor in ventromedial hypothalamus (VMH) neurons, activating proteins that inhibit the synthesis of epinephrine, thereby inhibiting sympathetic activity. The reduced sympathetic tone is relayed to osteoblasts via an adrenergic receptor, resulting in decreased resorption and increased bone formation. Conversely, inhibition of serotonin release from the DRN facilitates resorption and bone loss.