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Late-Life Depressive Symptoms Are Associated With Both Hyperactivity and Hypoactivity of the Hypothalamic-Pituitary-Adrenal Axis

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Editor: I read with great interest the paper of Penninx et al.¹ who investigated urinary free cortisol (UFC) excretion in older persons and studied the relationship between UFC excretion and late-life depressive symptoms. However, a shortcoming of their investigation makes the interpretation of their results difficult and their statement on the value of UFC measurements unfounded: the authors ignored the possible influence of variation in urine volume on UFC values. It may be remembered that Lloyd² stated more than 50 years ago that “we have also noticed that higher urine volume tends to be associated with higher corticosteroid levels. We have never found a patient with a low corticosteroid level who has a high urine volume” (p. 469). Taking into account the fact his so-called “corticosteroids” mainly comprise UFC and urinary free cortisone, we can assume that UFC excretion depends on urine volume. This assumption was strongly supported by recent human studies and earlier animal work.³ A possible explanation for this relationship was given by Findling and Raff⁴: “Because most filtered cortisol is metabolized or reabsorbed, increased fluid intake resulting in increased urine volume may reduce the fraction of filtered cortisol that is metabolized or reabsorbed, thereby increasing urine free cortisol excretion” (p.733).

In my opinion, interpretation of UFC excretion is only possible if person's fluid intake is strictly controlled and urine volume is considered an important preanalytical parameter. This may be especially true if UCF excretion is studied in persons with drinking behavior that vary with respect to fluid volume and time of fluid intake.

References

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