

recommendation for maximum salt intake of 6.0 grams of salt per day set by the Dutch Health Council<sup>10</sup> and slightly above the recommendation for a maximum intake of 5.0 grams of salt per day set by the World Health Organization.<sup>11</sup> However, when comparing the median intake of the PREVEND study of 8 grams per day (equivalent to 137 mmol of sodium per day) with the global mean intake of salt of approximately 10 grams per day (equivalent to 168 mmol of sodium per day),<sup>9</sup> we can conclude that the intake of sodium in the PREVEND study is relatively low. One might suppose that the association observed between low intake of sodium and risk of stroke may be explained by reverse causality, wherein a change in dietary choices is prompted by disease status. However, at baseline we already excluded subjects with history of cardiovascular disease, and, in sensitivity analyses, we tried to limit the chance of reverse causality by excluding all subjects with malignancies, type 2 diabetes, and chronic kidney disease at baseline. Exclusion of these patients did not materially change the results (hazard ratio [HR] per 1 standard deviation [SD] [51 mmol/24h] decrement, 1.45; 95% confidence interval [CI], 1.10-1.92), making reverse causality unlikely. However, as our study is observational in nature, reverse causality cannot completely be ruled out.

Third, we agree with Drs Musso and Dotto that sodium intake is closely linked to potassium intake and that high potassium has protective cardiovascular effects. For this reason, we included 24-hour urinary potassium excretion as a marker of potassium intake and as a potential confounder in the survival analyses (multivariable adjusted model 3). The association of low sodium intake with increased risk of

stroke remained independent of adjustment for urinary potassium excretion (HR per 1 SD [51 mmol/24h] decrement, 1.44; 95% CI, 1.14-1.82), supporting the notion that the increased risk of stroke observed is not due to harm induced by low potassium intake.

Fourth, the same holds true for adjustments for blood pressure and use of antihypertensive medication. We examined whether these variables were potential mediators of the association between sodium intake and stroke by including these variables in the multivariable model. However, the association of UNaV with risk of stroke remained materially unchanged (HR per 1 SD [51 mmol/24h] decrement, 1.47; 95% CI, 1.14-1.89). We therefore did not include these variables in the model on which Figure 1 is based, as these variables did not materially influence the association between urinary sodium intake and risk of stroke.

We thank Drs Musso and Dotto for appraising our paper as the first to correctly address a possible inverse association between sodium intake and risk of stroke and agree that, as in any study of observational nature, a risk of residual confounding will remain. As Drs Musso and Dotto implicitly suggest, more and higher-quality evidence on potential harmful effects of low sodium intake is certainly needed.

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Mona Lisa Decrypted:  
 Another Premise



**To the Editor:** In the September 2018 issue of *Mayo Clinic Proceedings*, Mehra and Campbell<sup>1</sup> gave a lovely and elegant review of the Mona Lisa painting and posited a medical explanation for the mystery of the lady as painted by the great master Leonardo da Vinci. Their insights tied hypothyroidism with attendant hyperlipidemia, lipoma, and xanthelasma as the cause of the enigmatic smile and her gaze. There is merit to this diagnosis, and this should be heavily weighted in the differential diagnosis analysis. Other analysts have attributed this to neurosyphilis,<sup>2</sup> postpartum Bell's palsy,<sup>3</sup> dentition

problems,<sup>3</sup> hyperlipidemia,<sup>4</sup> and strabismus.<sup>3</sup>

While painting a study of the great master as a learning exercise, several elements of the composition led me to consider other possibilities for the differential diagnosis.

Bruno Mottin, the curator of the Center for Research and Restoration of Museums of France, and a Canadian team imaged the painting using a new 3-dimensional technology. They noted that the initial da Vinci painting had the left hand “in a clenched rather than relaxed position.” This was later changed to a looser grasp “as if she was going to get up from a chair.”<sup>5</sup> The first iteration would most likely reflect the reality of the moment more accurately.

I submit that the position of the left arm and hand is more in keeping with paresis, which could be recent or from earlier in her life. The position of the right hand is one of support and is resting after positioning the left side. The flexion of the left hand is consistent with a neurological insult.

A basilar artery event would tie in hemiparesis of the left arm as well as the intriguing eye and smile effects. A brainstem lesion in the area of the pons could affect the motor nucleus of cranial nerve VII and the cranial nerve V nucleus as well as affect a large bundle of motor tracts. This would encompass the enigmatic gaze, the muscles for mysterious smiling and emotion, and paresis and support of the arm and hand.<sup>6</sup>

Brainstem artery occlusions are a subset of the posterior circulatory vascular events accounting for 1% to 4% of these strokes. Emboli, intrinsic basal artery atherosclerosis, and

penetrating small artery diseases are the common causes of this event. Embolic causes are more common in younger individuals.<sup>7</sup> Much rarer etiologies are vasculitis, trauma, and infectious processes including neurosyphilis.<sup>7-13</sup>

I also submit that the position of the lesion of the right wrist is more in keeping with a ganglion cyst than a lipoma.

The authors have written a wonderful review. Although hypothyroidism may very well be a part of the Mona Lisa story, there may be additional factors to consider in the differential diagnosis.

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In reply—The Mona Lisa  
Decrypted: Another  
Premise



The intrigue of the Mona Lisa continues to inspire as Dr Mullany provides yet another explanation for the enigmatic picture. Given the vast number of differential diagnoses already proposed previously and enumerated in our review,<sup>1</sup> this new assertion that a neurological injury or central nervous system malady defines the observed posture does deserve some discussion. Whether you examine the main painting or the deciphered one as interpreted by Bruno Mottin a decade ago,<sup>2</sup> the positions of the hands do not clearly advise in favor of a clear neurological insult. The painting was assuredly done with multiple sittings and not a single one and thus it is understandable that Leonardo da Vinci captured multiple phases and ended with what he thought was the most relaxed posture. The position of the right hand is consistent with a relaxed posture and even one that denotes some degree of flaccidity as would be encountered with hypothyroidism. To postulate a diagnosis of a neurovascular insult is beyond the depictions visually apparent and would likely be a bit of a stretch based on observed findings, although it