Working memory in women with polycystic ovary syndrome

Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy in reproductive-age women. Although many studies have focused on the metabolic and reproductive comorbidities associated with PCOS, few have examined brain functioning in this population. In this issue of *Fertility and Sterility*, Remi Soleman and his team at VU University Medical Center in the Netherlands explored working memory in women with PCOS and the effect of antiandrogen therapy on cognitive function by means of a functional magnetic resonance imaging (fMRI) case-control study (1). This novel approach showed increased activation in brain regions affecting storage of working memory and attentional processes in PCOS women compared with control women. Interestingly, these activation differences resolved with hormonal treatment.

The strengths of this study are threefold. First, Soleman et al. used fMRI to evaluate central processing while performing a working memory task. This is superior to previous studies which compared performance on various cognitive tasks before and after antiandrogen therapy (2, 3). Although these studies did suggest that hyperandrogenism associated with PCOS impaired some female-favoring cognitive tasks (such as verbal fluency), other tasks (such as verbal memory, manual dexterity, and visuospatial working memory) did not have consistent results. Because regional activation patterns differ by sex during working memory tasks (4), fMRI is an excellent modality for assessing the effect of androgens on cognitive functioning in women with PCOS. Second, they performed a multivariate regression analysis to correlate serum androgen levels (A, T, and DHEAS) with brain activity in the superior temporal lobe, superior parietal lobe, and inferior parietal lobe. Although they did not find correlation between serum androgen levels and regional activation during the working memory task, the absence of activation differences after cyproterone acetate and combined oral hormonal contraceptive suggested improved neuronal processing with hormonal treatment. Third, Soleman et al. used a cognitive task to extend the findings of activation pattern differences between PCOS women at baseline and control women. In PCOS women, hormonal treatment decreased the number of errors made while performing cognitive task, suggesting improved executive functioning. Although it is difficult to tell if cognitive processing improved because of cyproterone acetate treatment of hyperandrogenism alone or because of the addition of combined oral contraceptive (control women did not take combined oral contraceptive pills), hormonal treatment did affect both regional activation with N-back task and cognitive task performance.

It is notable that PCOS women had increased activation of regions of brain associated with cognitive processing while performing the working memory task. Although women with PCOS had similar performance on this complex working memory task compared with control women, increased activation was seen in the superior temporal and superior and inferior parietal lobes. This suggests that women with PCOS need additional neuronal recruitment to perform the same cognitive tasks compared with non-PCOS women. What this means for performance of daily activities is unclear. On the one hand, women with PCOS seem to have equivalent cognitive function. However, recruitment of additional cognitive processing regions may reduce overall efficiency or strain neuronal resources.

The Soleman et al. study highlights the need for innovative research in understanding the central mechanisms underlying PCOS. We now understand that women with PCOS may use and recruit additional neurons to perform the same cognitive tasks compared with non-PCOS women. Because serum androgen levels did not correlate with activation differences seen with central processing, future studies exploring the effects of metabolism and sleep on cognitive processing may be useful. Furthermore, hormonal therapy may have additional benefits that extend to improved cognition, although it is unclear at this time if antiandrogen or combined oral contraceptive therapy is associated with this improvement. This study is an exciting step forward in understanding the full phenotype and underlying pathophysiology in women with PCOS. Continued studies exploring interaction between hormonal milieu and central processing are needed to further our understanding of this complex disease.

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