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Cognitive Function in Reproductive Aged Individuals with Polycystic Ovary Syndrome

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PCOS by Rotterdam criteria is defined by the presence of at least two of the following: oligomenorrhea, hyperandrogenism and polycystic ovaries. Although not required for diagnosis, PCOS often has metabolic manifestations, particularly insulin resistance. In studies of non-PCOS populations, it appears a nexus may exist between insulin resistance and neuropsychological outcomes, such as cognitive performance (particularly executive function skills), cognitive aging, and depression. Cognitive performance, such as verbal and spatial skills, may also be impacted by gonadal hormones. It is therefore surprising that the relationship between PCOS and neuropsychological outcomes has been only minimally investigated. This study was therefore designed to measure and compare cognition in Rotterdam-PCOS subjects with and without hyperandrogenism and to test the hypothesis that executive function performance (cognitive control, verbal fluency and working memory) is lower in those with hyperandrogenism. **Methods:** Forty-eight sequential subjects with PCOS were recruited from a multi-disciplinary PCOS clinic. Those with clinical/biochemical hyperandrogenism (in addition to oligomenorrhea/polycystic ovaries) were designed "NIH-PCOS" (n=35); while those without hyperandrogenism (only oligomenorrhea and polycystic ovaries) were designated "non-androgenic PCOS" (n=13).

Neuropsychological test administration and scoring were performed by trained personnel. Verbal and perceptual reasoning were measured with Wechsler Adult Intelligence Scale (WAIS); memory was measured by California Verbal Learning Trials (long delay recall), and processing speed by WAIS symbol search. Executive functions were measured with Delis-Kaplan System: Stroop and Trail Making (cognitive control); Design and Verbal Fluency (generativity); WAIS: Digit Span (working memory); and Weschler Memory Scale: Symbol Span (working memory). Sample-based z-scores were calculated for cognitive outcomes. We compared z-scores using linear regressions, adjusting for age, race, and years of education. A composite executive function score was calculated as the mean z-score on all six executive function tests. **Results:** Groups were similar for age and BMI, but NIH-PCOS showed greater mean (SD) Homa-IR (4.2 (6.1) vs. 1.82 (1.9); p=.06), compared to non-androgenic PCOS. Cognitive performance was similar for measures of "pre-morbid" IQ, including verbal and perceptual reasoning, memory and processing speed. However, subjects with NIH-PCOS demonstrated lower relative performance for executive functions (β-coefficient for executive function composite z-score: -0.44, 95% CI: -0.79, -0.09; p=0.016). Subdomains showing decreased performance (β-coefficient) included verbal fluency (-0.62; p=.04), working memory (-0.75; p=.04) and cognitive control (-0.53; p=.05). We additionally assessed cognitive performance in relation to insulin resistance (Homa >2.1). Considering non-androgenic PCOS without insulin resistance as referent, NIH-PCOS subjects with insulin resistance showed the lowest performance on the executive function composite score, followed by those with NIH-PCOS without insulin resistance (p-trend = .001). **Conclusion:** People with hyperandrogenic PCOS may experience challenges in executive functioning compared to non-androgenic counterparts. Additional research is needed to confirm findings in larger cohorts and to investigate the role of modifiable factors.

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