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REVIEWER'S REPORT

Manuscript No.: IJAR-53634 Date: 30/08/2025

Title: Genetic and Neuropeptide Aspects in Central Precocious Puberty (CPP)

Recommendation:
✓ Accept as it is .....
Accept after minor revision.....
Accept after major revision .....
Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality		✓		
Techn. Quality		✓		
Clarity		✓		
Significance	✓			

Reviewer Name: Dr. S. K. Nath Date: 30/08/2025

Reviewer's Comment for Publication:
This review effectively synthesizes recent advances in understanding the genetic and neuropeptidergic mechanisms underlying CPP. It underscores the importance of integrating molecular genetics and neuroendocrinology into diagnostic and therapeutic strategies, paving the way for personalized medicine in pediatric endocrinology. Future research should focus on validating novel biomarkers, exploring targeted therapies, and understanding long-term outcomes to optimize care for individuals with CPP.

Reviewer's Comment / Report

Strengths

1. **Comprehensive Integration:** The paper successfully combines insights from genetic studies, neuroendocrinology, and clinical diagnostics, offering a holistic view of CPP etiologies.
2. **Focus on Genetic Markers:** Highlights key genes like MKRN3 and DLK1, providing detailed mechanistic insights into their roles in pubertal timing.
3. **Emerging Biomarkers:** Emphasizes the potential of neuropeptides such as kisspeptin and neurokinin B as biomarkers, which could improve diagnostic accuracy and treatment monitoring.
4. **Future Directions:** Outlines promising areas, including genomic technologies, individualized therapies, and the development of neuropeptide modulators, guiding future research.
5. **Clinical Relevance:** Connects molecular mechanisms with clinical applications—diagnosis, prognosis, and therapeutics—making the review valuable for clinicians.

Weaknesses

1. **Lack of Quantitative Data:** The review summarizes findings but offers limited quantitative analysis, such as prevalence rates or statistical validation of genetic markers, which could strengthen its conclusions.
2. **Limited Discussion on Long-term Outcomes:** While it mentions the importance of long-term psychosocial and metabolic outcomes, detailed data or longitudinal studies are not extensively discussed.
3. **Therapeutic Limitations Not Fully Explored:** Emerging therapies like kisspeptin antagonists are mentioned, but there is little critique or discussion of current limitations and challenges in implementing these treatments.
4. **Potential Bias Towards Genetic Factors:** The focus on genetics might overshadow environmental and epigenetic factors that also significantly influence pubertal timing.
5. **Absence of Visual Aids:** The review could have benefited from diagrams or tables summarizing gene functions, pathways, or diagnostic algorithms for clarity.