Reviewer's report

Title: Ubiquitous Neurocognitive Dysfunction in Familial Adenomatous Polyposis: Proof-of-Concept of the role of APC Protein in Neurocognitive Function.

Version: 0 Date: 06 Jan 2020

Reviewer: Rolf Sijmons

Reviewer's report:

This paper looks into the neurocognitive function of FAP patients, showing that matched controls outperform individuals with germline APC mutations in several areas. Although there is some theoretical and animal study basis to expect cognitive dysfunction caused by lack of normal APC, there is hardly any literature on cognition in FAP patients available. I therefore appreciate the initiative to perform this study. Although the number of patients studied is relatively small, methods and statistics including multiple-testing correction are appropriate and the results, when confirmed by other studies, may help us to further support FAP families.

One small comment:

the authors wonder (page 18) whether the medical and psychosocial circumstances of having a (i.e. any) hereditary tumor syndrome can act as a confounder in studies on cognitive function. I agree, but I suggest that their examples of Lynch and hereditary breast and ovarian cancer syndromes would not make the most ideal group to compare with FAP as these 2 syndromes start their surveillance and interventions &gt;=(20-)25yrs and not already in childhood as is the case for FAP. The authors could therefore 'refine' their remark a bit.

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