

Title: Pediatric intestinal motility disorders

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The manuscript has been improved according to the suggestions of reviewers:

Revisions has been made according to the suggestions of the editor/reviewers

(1) Editor

Insert postal codes.

Has been done

Create audio file for core tip.

Has been created.

(2) Reviewer 03011198

„Author explained about pediatric intestinal motility disorders. Good summary about this field. Providing figures and tables of each disease may help readers.“

Thank you for this favorite review. Figures are now included in the manuscript. Tables are not added, since the space in this review is limited.

(3) Reviewer 03252920

„This is a very interesting manuscript that discusses relevant aspects regarding intestinal motility disorders in childhood. However, some aspects are covered in a very superficial way, especially those related to diagnosis, such as anorectal manometry, barium enema and about new adjuvants methods in the histopathological analysis of rectal biopsies, such as calretinin immunohistochemistry. In addition, another aspect that could have been discussed is the presence of alarm signals for organic causes of constipation, which represent a key step in the clinical evaluation of these children. In my opinion, these points could be better addressed by the authors.“

Thank you for the review and the valuable criticism.

We have now included the other diagnostic tools, i.e. contrast studies and anorectal manometry. Specificity and Sensibility of these methods has been added to the manuscript.

Furthermore we included a short paragraph on new histopathological stainings as calretinin, peripherin and S-100.

Alarm signals for organic causes are the delayed passage of meconium and severe ongoing constipation, which requires complex treatment including surgery.

This information has been included in the text.

(4) Reviewer 03260896

„An interesting paper concerning motility disorders in children. It would improve the quality of the paper if in the diagnosis section more emphasis was laid upon imaging techniques. One of the conclusions the authors state is that there have been advances in diagnostic methods, however they are not mentioned. For example: does anal manometry have a role in this? What I also miss is how and when to make the distinction between "normal" functional motility disorders and underlying pathology. Maybe the authors could comment on that. Last comment: what is the consequence of accurate diagnosis in childhood constipation for prognosis in adulthood?“

Thank you for the valuable comments.

We have described the main imaging studies in the manuscript. Anorectal manometry has improved its diagnostic accuracy and is regarded an advanced method. Further advances have been reached with new staining methods.

The distinction between functional motility problems and true underlying pathology could be made usually early due to the typical history and specific findings in the diagnostics. Most of the patients with HD will be diagnosed in newborn or infant period.

Accurate diagnosis in childhood allows usually a good prognosis in adulthood.

(5) Reviewer 00055279

„This is an excellent paper showing in great detail pediatric intestinal motility disorders. If authors provide images from immunohistochemical studies by authors or other investigators, it would greatly help readers understanding. In addition, current (or potential) in vivo imaging methods need to be discussed.“

Thank you for your comments. We have now included representative images in the manuscript.

In regards to the in vivo imaging methods there are only few experimental approaches with no clinical relevance so far.