**Title of the project:** The influence of experimental gastrointestinal injury and inflammation on pharmacokinetics of Alzheimer disease drugs

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<th>Summary of 2018 results</th>
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**Title of the presentation:** The effect of a single and repeated doses of memantine on gastric myoelectric activity in experimental pigs  
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Memantine, currently available for the treatment of Alzheimer's disease, is an uncompetitive antagonist of the N-methyl-D-aspartate type of glutamate receptors. In humans, memantine administration is associated with different gastrointestinal dysmotility side effects (vomiting, diarrhoea, constipation, motor-mediated abdominal pain), thus limiting its clinical use. Mechanism of these motility disorders has not been clarified yet. Pigs can be used in various preclinical experiments due to their relatively very similar gastrointestinal functions compared to humans. The aim of this study was to evaluate the impact of a single and repeated doses of memantine on porcine gastric myoelectric activity evaluated by means of electrogastrography (EGG). Six adult female experimental pigs (mean weight 41.7±5.0 kg) entered the study for two times. The first EGG was recorded after a single intragastric dose of memantine (20 mg). In the second part, EGG was accomplished after 7-day intragastric administration (20 mg per day). All EGG recordings were performed under general anaesthesia. Basal (15 minutes) and study recordings (120 minutes) were accomplished. Results were expressed as dominant frequency of gastric slow waves (DF) and power analysis (areas of amplitudes). Single dose of memantine significantly increased DF, from basic values (1.65±1.05 cycles per min.) to 2.86 cpm after 30 min. (p=0.008), lasting till 75 min. (p=0.014). Basal power (median 452; inter-quartile range 280 – 1312 μV^2) raised after 15 min. (median 827; IQR 224 - 2769; p=0.386; NS), lasting next 30 min. Repetitively administrated memantine caused important gastric arrhythmia. Both single and repeated doses of memantine increased DF. Severe gastric arrhythmia and long-lasting low power after repeated administration might explain possible gastric dysmotility side effects in the chronic use of memantine.

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