

## A POSSIBLE ROLE OF GUT MICROBIOTA IN THE BEHAVIORAL CONTROL OF ALCOHOL-DEPENDENT SUBJECTS

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**Background:** In a recent study, we have shown that clinical symptoms of alcohol dependence such as depression and alcohol-craving were related to increases in gut permeability and in inflammation. These observations suggest that the gut could influence behavior. However, the nature of the intestinal processes involved in the change in gut permeability and in inflammation and their relation to psychological symptoms is still unknown.

**Subjects and methods:** We compared 13 non-cirrhotic alcohol-dependent (AD) subjects hospitalized for a detoxification program with 15 healthy controls matched for age, sex and BMI. Gut permeability was measured using <sup>51</sup>Cr-EDTA. Fecal samples were collected to analyze the gut microbiota composition (using pyrosequencing and qPCR) and metabolomic analysis (GC/MS) was used to assess the gut microbiota function. The inflammatory pathways that were stimulated by gut-derived bacterial products were also analyzed in peripheral blood mononuclear cells (PBMC) at the mRNA level. We also used self-reported questionnaires to assess the psychological symptoms of these patients (depression (BDI), anxiety (STAI) and alcohol craving (OCDS)). The analyses were performed twice, at the first day of alcohol withdrawal and after 18 days of abstinence.

**Results:** Gut permeability was higher in AD subjects and was associated with specific alterations in the gut microbiota composition and function. The leaky gut allowed the translocation of gut-derived bacterial toxins such as lipopolysaccharides (LPS) and peptidoglycans (PGN) to the systemic circulation. Correlation analyses revealed that the gut permeability was strongly related to psychological symptoms of alcohol-dependence, at both times of withdrawal. The bacterial toxins simulated their Toll-like receptors in PBMCs and activated specific inflammatory pathways that were found to correlate with alcohol-craving. The alcohol withdrawal induced a decrease in gut permeability and in LPS-associated inflammatory pathways. However, 18 days of abstinence did not restore the gut microbiota composition, except in some specific species.

**Conclusion:** These observations suggest that alterations at the level of the gut microbiota influence the gut permeability and activate specific inflammation pathways that are related to psychological symptoms of alcohol-dependence. Altogether these observations are consistent with a role of inflammation as one mediator of a gut-brain communication in AD patients.

**Key words:** alcohol-dependence - gut microbiota – inflammation - intestinal permeability - alcohol-craving

## SENSORY PROCESSING IN YOUNG PATIENTS WITH AUTISM SPECTRUM DISORDERS (ASDs): A STUDY OF THE CORRELATION BETWEEN THE SENSORY PROFILE AND THE CLINICAL EVOLUTION OF THE ASDS

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**Background:** Sensory abnormalities have been reported since the first descriptions of ASDs. In the last years an increasing interest in these symptoms has arisen, around the question of their possible part in the physio- and psychopathology of autism as well as their potential use as early alerting signs. They have been recently added to the diagnostic criteria of the DSM-5. This on-going study investigates the relation between sensory processing anomalies and the social/communication symptoms in ASDs in a twofold design.

**Subjects and methods:** The cross-sectional part of the study investigates the patterns of sensory abnormalities in 50 children with ASDs (age 2.5 to 5 years) assessed with the Sensory Profile questionnaire. As secondary outcomes, we are looking for differences between these patterns in the severity of social and communication symptoms (social affect score in the ADOS, Vineland Adaptive Behavior Scale) and in the global development impairment (PEP-R). Among these children, those aging 2.5 to 3.5 years will be enrolled in a follow-up study. The different measures will be repeated after two years, to show whether different clinical trajectories can be observed and whether they are associated with different sensory patterns in the initial clinical presentation.

**Results:** First results of the cross-sectional part reveal that different patterns of sensory anomalies are correlated to different degrees in the severity of ASDs and tend to discriminate different populations in children with ASDs.

**Conclusions:** Sensory anomalies are core symptoms of ASDs and are an essential parameter in the early evaluation process of very young children with ASDs.

**Keywords:** autism – sensory – severity - early signs

## NEUROLEPTIC MALIGNANT-LIKE SYNDROME AFTER SURGERY IN A PATIENT TAKING LEVODOPA

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**Background:** We present a case of a patient with symptoms indicative of neuroleptic malignant syndrome after sudden dopaminergic agents withdrawal.

**Subjects and methods:** A search of the literature up to December 2013 was performed using the MEDLINE search engine. English-language articles, with no restriction regarding the type of articles, were identified using the search terms: levodopa withdrawal, neuroleptic malignant-like syndrome, neuroleptic malignant syndrome, Parkinson's disease.

**Results:** A 85-years old male patient with an history of Parkinson's disease was admitted via the emergency department for an Acute abdomen and subsequently found to have appendicitis. Following the emergent Appendectomy his usual dopaminergic agents (l-dopa - pramipexole) were held due to complications following the surgery. The consultation/liaison psychiatrist was called following agitation and acute confusion. Upon examination the patient was found to have acute confusion, fever of 39°C, rigidity, elevated creatinine kinase (>2000 UI/L) and acute renal impairment due to rhabdomyolysis. The symptoms were consistent with neuroleptic malignant-like syndrome (NMLS) likely associated to L-dopa withdrawal. The patient was immediately transferred to the Intensive Care Unit where Nasogastric L-Dopa was the therapy that was initiated.

**Conclusions:** We want to underline the importance of the pathophysiological mechanism that implies the reduction of availability of dopamine for the D-2 receptors, that can follow the interruption of dopaminergic medication in patients suffering of Parkinson's disease. Early recognition and quick decision making can increase the outcomes of a condition that still has a fatal potential. We believe that this can be a useful tool for consultation/liaison psychiatrists in the general hospital.

**Key words:** levodopa - neuroleptic malignant-like syndrome - substance withdrawal syndrome