centre de Ressources Autisme RHÔNE-ALPES

Bibliographie : TSA / Douleur (2019-2021)

Références classées par ordre chronologique décroissant.

1. Siper Paige M., Layton Christina, Levy Tess, Lurie Stacey, Benrey Nurit, Zweifach Jessica, Rowe Mikaela, Tang Lara, Guillory Sylvia, Halpern Danielle, Giserman-Kiss Ivy, Del Pilar Trelles Maria, Foss-Feig Jennifer H., De Rubeis Silvia, Tavassoli Teresa, Buxbaum Joseph D., Kolevzon Alexander. **Sensory Reactivity Symptoms Are a Core Feature of ADNP Syndrome Irrespective of Autism Diagnosis**. *Genes*. 2021; **12**(3).

Background: Activity dependent neuroprotective protein (ADNP) syndrome is one of the most common single-gene causes of autism spectrum disorder (ASD) and intellectual disability, however, the phenotypes remain poorly described. Here we examine the sensory reactivity phenotype in children and adolescents with ADNP syndrome. Methods: Twenty-two individuals with ADNP syndrome received comprehensive clinical evaluations including standardized observations, caregiver interviews, and questionnaires to assess sensory reactivity symptoms. Relationships between sensory symptoms and age, sex, ASD, IQ, and adaptive behavior were examined. Genotype-phenotype correlations with the recurrent p.Tyr719* variant were also explored. Results: Sensory reactivity symptoms were observed and reported in all participants. A syndrome-specific phenotype was identified, characterized by high levels of sensory seeking across tactile, auditory, and visual domains. Tactile hyporeactivity, characterized by pain insensitivity, was reported in the majority of participants. Sensory symptoms were identified across individuals regardless of age, sex, IQ, adaptive ability, genetic variant, and most importantly, ASD status. No significant differences were identified between participants with and without the recurrent p.Tyr719* variant on any sensory measure. Conclusions: Sensory reactivity symptoms are a common clinical feature of ADNP syndrome. Quantifying sensory reactivity using existing standardized measures will enhance understanding of sensory reactivity in individuals with ADNP syndrome and will aid in clinical care. The sensory domain may also represent a promising target for treatment in clinical trials.

2. Saravane D., Mytych I. **Douleur et autisme**. *Douleur et Analgésie*. 2021; (Preprints): 1-12.

L'autisme, trouble neurodéveloppemental est caractérisé par des altérations sociocommunicatives, la présence de comportements stéréotypés et d'intérêts restreints. Jusqu'à une période récente, les personnes atteintes de trouble du spectre autistique (TSA) étaient considérées comme insensibles à la douleur. Les spécificités du fonctionnement

autistique incluent des problèmes sensoriels qui, associés aux déficit cognitif et particularités communicationnelles, interrogent sur la nature réelle du lien existant entre la douleur et l'autisme. Les données de la littérature, peu nombreuses, mettent en évidence chez les autistes une hypersensibilité à la stimulation douloureuse et des modalités d'expression atypiques de la douleur. Ces éléments de compréhension, établissant notamment un lien entre comportement-problème et douleur, doivent nous permettre de repérer, évaluer, traiter la douleur et réduire les comportements-problèmes de ces personnes présentant un TSA. À partir des donnés, une méthode d'évaluation clinique spécifique de la douleur et des échelles ont pu être mises en place.

3. Ruelle-Le Glaunec Lucien, Inquimbert Perrine, Hugel Sylvain, Schlichter Rémy, Bossu Jean-Louis, Ruelle-Le Glaunec Lucien, Inquimbert Perrine, Hugel Sylvain, Schlichter Rémy, Bossu Jean-Louis. **Nociception, douleur et autisme**. *Médecine/Sciences*. 2021; **37**(2): 141-51.

Les sujets autistes présentent fréquemment des anomalies sensorielles. Celles concernant la nociception ainsi que sa potentielle résultante, la douleur, sont d'un intérêt capital. En effet, du fait de nombreuses comorbidités, les sujets autistes sont plus souvent exposés à des situations douloureuses que la population générale. Alors qu'ils sont souvent considérés comme moins sensibles, les études expérimentales sur ce point sont loin de faire consensus. Utiliser des modèles animaux pourrait permettre de s'affranchir de certaines sources de variabilité et d'apporter, dans le cadre de l'autisme, une vue d'ensemble des altérations potentielles du système nociceptif aux niveaux cellulaire et moléculaire.

4. Palese Alvisa, Conforto Ludovica, Meloni Francesca, Bordei Valeria, Domenighini Alessia, Bulfone Elena, Grassetti Luca, Gonella Silvia. **Assessing pain in children with autism spectrum disorders: findings from a preliminary validation study**. *Scandinavian journal of caring sciences*. 2021; **35**(2): 457-67.

Aims: Assessing pain in children with autism spectrum disorders (ASDs) can be extremely challenging, since many cannot self-report pain. This study aims to test the validity of the Non-Communicating Children's Pain Checklist - Revised (NCCPC-R) in identifying pain in children and adolescents affected by ASDs.; Materials and Methods: A two-phase validation study based on (a) the translation and cultural adaptation of the NCCPC-R to Italian and to ASD-specific needs and context; and (b) the validation of a modified, 32-item version of the NCCPC-R. In all, 141 carers of children aged 6-16 years with ASDs were asked to recall an in-pain episode and a not-in-pain episode of their child and to rate on a 3-point scale (0 = not at all, 3 = very often) each behaviour included in the tool. Internal consistency (Cronbach's α), explorative and confirmative factorial structure, as well as concurrent and discriminant validity, were all assessed.; Results: Confirmatory factor analysis established the revised version of the NCCPC-R for children with ASDs (named = NCCPC-R ASD), formed from 10 of the original 30 items categorised into three factors ('Changing in mood', 'Increasing in tension' and 'Alerting reaction') to have an acceptable level of reliability. The tool was internally consistent (α = 0.741 during in-pain episodes, α = 0.790 during not-in-pain episodes) and was able to discriminate between in-pain episodes (13.36 out of 40; CI 95% 12.34-14.39) and not-in-pain episodes (7.84 out of 40; CI 95% 6.86-8.82, $p < 0.001$).; Conclusions: These results provide preliminary evidence that the 10-item version of the NCCPC-R ASD is a reliable and valid tool for assessing pain in children with ASD.

5. Messmer Rosemary, Nader Rami, Craig Kenneth. **Brief Report: Judging Pain Intensity in Children with Autism Undergoing Venepuncture: The Influence of Facial Activity**. *Journal of Autism and Developmental Disorders*. 2021; (Preprints): 1-4.

Abstract: The biasing effect of pain sensitivity information and the impact of facial activity on observers' judgements of pain intensity of children with autism were examined. Observers received information that pain experience in children with autism is either the same as, more intense than, or less intense than children without autism. After viewing six video clips of children with autism undergoing venepuncture, observers estimated pain intensity using a visual analogue scale. Facial activity as coded by Chambers et al. (Child Facial Action Coding System Revised Manual, 1996) had a significant impact on observers' estimates of pain intensity; pain sensitivity information did not. These results have important implications for the assessment and management of pain in children with autism.

6. Marbach Felix, Stoyanov Georgi, Erger Florian, Stratakis Constantine A., Settas Nikolaos, London Edra, Rosenfeld Jill A., Torti Erin, Haldeman-Englert Chad, Sklirou Evgenia, Kessler Elena, Ceulemans Sophia, Nelson Stanley F., Martinez-Agosto Julian A., Palmer Christina G. S., Signer Rebecca H., Andrews Marisa V., Grange Dorothy K., Willaert Rebecca, Person Richard, Telegrafi Aida, Sievers Aaron, Laugsch Magdalena, Theiß Susanne, Cheng YuZhu, Lichtarge Olivier, Katsonis Panagiotis, Stocco Amber, Schaaf Christian P. **Variants in PRKAR1B cause a neurodevelopmental disorder with autism spectrum disorder, apraxia, and insensitivity to pain**. *Genetics in medicine : official journal of the American College of Medical Genetics*. 2021; **23**(8): 1465-73.

Purpose: We characterize the clinical and molecular phenotypes of six unrelated individuals with intellectual disability and autism spectrum disorder who carry heterozygous missense variants of the PRKAR1B gene, which encodes the R1β subunit of the cyclic AMP-dependent protein kinase A (PKA).; Methods: Variants of PRKAR1B were identified by single- or trio-exome analysis. We contacted the families and physicians of the six individuals to collect phenotypic information, performed in vitro analyses of the identified PRKAR1B-variants, and investigated PRKAR1B expression during embryonic development.; Results: Recent studies of large patient cohorts with neurodevelopmental disorders found significant enrichment of de novo missense variants in PRKAR1B. In our cohort, de novo origin of the PRKAR1B variants could be confirmed in five of six individuals, and four carried the same heterozygous de novo variant c.1003C>T (p.Arg335Trp; NM_001164760). Global developmental delay, autism spectrum disorder, and apraxia/dyspraxia have been reported in all six, and reduced pain sensitivity was found in three individuals carrying the c.1003C>T variant. PRKAR1B expression in the brain was demonstrated during human embryonal development. Additionally, in vitro analyses revealed altered basal PKA activity in cells transfected with variant-harboring PRKAR1B expression constructs.; Conclusion: Our study provides strong evidence for a PRKAR1B-related neurodevelopmental disorder.

7. Liu Jun, Chen Lucy L., Shen Shiqian, Mao Jianren, Lopes Maria, Liu Siyu, Kong Xuejun. **Challenges in the Diagnosis and Management of Pain in Individuals with Autism Spectrum Disorder**. *Review Journal of Autism and Developmental Disorders*. 2021; (Preprints): 1-12.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder associated with many systemic comorbidities, including sensory dysfunctions. A growing body of literature explored patients' unusually intense reactions to innocuous sensory stimuli but very little is known about ASD patients' response to noxious stimuli such as pain. Patients with ASD are thought to have low sensitivity to pain, but currently, there is no clear consensus on pain responsivity/sensitivity/expression in patients with ASD. Pain is likely a significant source of suffering for patients with ASD, but limited literature suggest that it may be underdiagnosed and undertreated, due to patients' potentially abnormal reaction to pain/pain expression, and their limited social communication skills. In this article, we first discuss the abnormalities in pain sensitivity and expression, two key obstacles in pain management for patients with autism. Next, we explore currently available tools in pain diagnosis for patients with autism. The third, we discuss pain management in autism patient with an emphasis on the perioperative setting where literature is most abundant. Last, we call for further research and offer suggestions for implementing better pain assessment and management protocols based on our understanding of this unique population.

8. Kurtz-Nelson Evangeline C., Tham See Wan, Ahlers Kaitlyn, Cho Daniel, Wallace Arianne S., Eichler Evan E., Bernier Raphael A., Earl Rachel K. **Brief Report: Associations Between Self-injurious Behaviors and Abdominal Pain Among Individuals with ASD-Associated Disruptive Mutations**. *Journal of autism and developmental disorders*. 2021; **51**(9): 3365-73.

Self-injurious behaviors (SIB) are elevated in autism spectrum disorder (ASD) and related genetic disorders, but the genetic and biological mechanisms that contribute to SIB in ASD are poorly understood. This study examined rates and predictors of SIB in 112 individuals with disruptive mutations to ASD-risk genes. Current SIB were reported in 30% of participants and associated with poorer cognitive and adaptive skills. History of severe abdominal pain predicted higher rates of SIB and SIB severity after controlling for age and adaptive behavior; individuals with a history of severe abdominal pain were eight times more likely to exhibit SIB than those with no history. Future research is needed to examine associations between genetic risk, pain, and SIB in this population.

9. Humphrey R., Finn D. P., Roche M. **P.206 Altered pain responding in a model of autism associated with changes in endocannabinoid system-related gene expression**. *European Neuropsychopharmacology*. 2021; **44**: S20-S.

10. Boerlage A. A., Sneep L., van Rosmalen J., van Dijk M. **Validity of the Rotterdam Elderly Pain Observation Scale for institutionalised cognitively impaired Dutch adults**. *Journal of intellectual disability research : JIDR*. 2021; **65**(7): 675-87.

Background: The Rotterdam Elderly Pain Observation Scale (REPOS) has not yet been validated for institutionalised cognitively impaired adults. To fill this gap of knowledge, we tested psychometric properties of the REPOS when used for pain assessment in this population.; Methods: In this multicentre observational study, residents were filmed during a possibly painful moment and at rest. Healthcare professionals were asked to rate residents' pain by means of a Numeric Rating Scale (NRS)-proxy. Two researchers assessed pain with the REPOS and the Chronic Pain Scale for Non Verbal Adults with Intellectual Disabilities (CPS-NAID) from

video-recordings.; Results: In total, 168 observations from 84 residents were assessed. Inter-observer reliability between the two researchers was good, with Cohen's kappa 0.72 [95% confidence interval (CI) 0.64 to 0.79]. Correlation between the REPOS and CPS-NAID for a possibly painful moment was 0.73 (95% CI 0.65 to 0.79). Sensitivity (85%) and specificity (61%) for the detection of pain were calculated with REPOS ≥ 3 and NRS ≥ 4 as a reference value. Item response theory analysis shows that the item grimace displayed perfect discrimination between residents with and without pain.; Conclusion: The REPOS is a reliable and valid instrument to assess pain in cognitively impaired individuals.

11. Balter Leonie J. T., Wiwe Lipsker Camilla, Wicksell Rikard K., Lekander Mats. **Neuropsychiatric Symptoms in Pediatric Chronic Pain and Outcome of Acceptance and Commitment Therapy**. *Frontiers in psychology*. 2021; **12**: 576943.

Considerable heterogeneity among pediatric chronic pain patients may at least partially explain the variability seen in the response to behavioral therapies. The current study tested whether autistic traits and attention-deficit/hyperactivity disorder (ADHD) symptoms in a clinical sample of children and adolescents with chronic pain are associated with socioemotional and functional impairments and response to acceptance and commitment therapy (ACT) treatment, which has increased psychological flexibility as its core target for coping with pain and pain-related distress. Children and adolescents aged 8-18 years (N = 47) were recruited. Patients and their parents completed questionnaires pre- and post-ACT of 17 sessions. Correlational analyses and mixed-effects models were used to assess the role of autistic traits and ADHD symptoms in pretreatment functioning and ACT-treatment response. Outcome variables were degree to which pain interfered with daily activities (i.e., pain interference, sleep, and physical and school functioning), socioemotional functioning (i.e., depressive symptoms, emotional, and social functioning), psychological inflexibility, and pain intensity. Autistic traits and ADHD symptoms, pain frequency, and pain duration were measured at pretreatment only. Higher autistic traits were associated with greater pain interference, higher depression, and greater psychological inflexibility. Higher ADHD symptomatology was associated with greater pretreatment pain interference, lower emotional functioning, greater depression, and longer duration of pain. Across patients, all outcome variables, except for sleep disturbances and school functioning, significantly improved from pre- to post-ACT. Higher autistic traits were associated with greater pre- to post-ACT improvements in emotional functioning and sleep disturbance and non-significant improvements in pain interference. ADHD symptomatology was not associated with treatment outcome. The current results showed that neuropsychiatric symptoms in pediatric chronic pain patients are associated with lower functioning, particularly pain interfering with daily life and lower socioemotional functioning. The results suggest that not only pediatric chronic pain patients low in neuropsychiatric symptoms may benefit from ACT, but also those high in autism traits and ADHD symptoms. With the present results in mind, pediatric chronic pain patients higher in autistic traits may actually derive extra benefit from ACT. Future research could assess whether increased psychological flexibility, the core focus of ACT, enabled those higher in autism traits to cope relatively better with pain-related distress and thus to gain more from the treatment, as compared to those lower in autism traits. Moreover, to address specific effects of ACT, inclusion of an appropriate control group is key.

12. **Questions posées au Docteur Djéa Saravane, à propos de douleur et autisme**. *Douleurs*. 2021; **22**(2): 104-6.

13. Vetri Luigi. **Autism and Migraine: An Unexplored Association?** *Brain sciences*. 2020; **10**(9).

Autism spectrum disorder is characterized by neurological, psychiatric and medical comorbidities-some conditions co-occur so frequently that comorbidity in autism is the rule rather than the exception. The most common autism co-occurring conditions are intellectual disability, language disorders, attention-deficit hyperactivity disorder, epilepsy, gastrointestinal problems, sleep disorders, anxiety, depression, obsessive-compulsive disorder, psychotic disorders, oppositional defiant disorder, and eating disorders. They are well known and studied. Migraine is the most common brain disease in the world, but surprisingly only a few studies investigate the comorbidity between autism and migraine. The aim of this narrative review is to explore the literature reports about the comorbidity between autism and migraine and to investigate the common neurotransmitter, immune, anatomical and genetic abnormalities at the base of these two conditions.

14. Vaughan Sarah, McGlone Francis, Poole Helen, Moore David J. **A Quantitative Sensory Testing Approach to Pain in Autism Spectrum Disorders**. *Journal of autism and developmental disorders*. 2020; **50**(5): 1607-20.

Sensory abnormalities in autism has been noted clinically, with pain insensitivity as a specified diagnostic criterion. However, there is limited research using psychophysically robust techniques. Thirteen adults with ASD and 13 matched controls completed an established quantitative sensory testing (QST) battery, supplemented with measures of pain tolerance and central modulation. The ASD group showed higher thresholds for light touch detection and mechanical pain. Notably, the ASD group had a greater range of extreme scores (the number of z-scores outside of the 95% CI > 2), dynamic mechanical allodynia and paradoxical heat sensation; phenomena not typically seen in neurotypical individuals. These data support the need for research examining central mechanisms for pain in ASD and greater consideration of individual difference.

15. Saravane Djea. **Effective management of pain in autism spectrum disorder and intellectual disability**. In: Incayawar M, Maldonado-Bouchard S, Clark MR, editors. *Overlapping pain and psychiatric syndromes: Global perspectives*. New York, NY: Oxford University Press; 2020. p. 357-68.

Research has shown that people with intellectual disability (ID) or autism spectrum disorder (ASD) have markedly higher rates of chronic medical conditions than do people in the general population. Relatively little empirical knowledge is available to guide our understanding and treatment of pain among people with ASD. Compounding this paucity of knowledge are notions that persons with ASD are insensitive or indifferent to pain. Several studies have reported insensitivity to pain in the autistic population compared with control groups, but the contribution of other factors that may partially explain the results is lacking. The altered perception of others derives from inadequate communication skills and social relatedness. Until clinical research is conducted using a rigorous methodology, the atypical expression of

pain raises the question of how to assess and manage pain in people with ASD, particularly when there are major communication disorders. The identification and assessment of pain is the responsibility of everyone, including those close to the person with ASD or ID, including family members, caregivers, and professionals. The management of pain must include the identification, when possible, of the painful pathology, its evaluation, and the preparation of treatment plans aimed at reducing problem behaviors.

16. Moulster Gwen. **Identifying pain in people who have complex communication needs**. *Nursing Times*. 2020; **116**(2): 18-21.

Assessing pain in people who have complex communication needs can be challenging and should include the opinions and experiences of the person's family and others who know the person well. This article describes an assessment approach, in which the learning disability nurse develops a pain picture showing how the patient is when healthy, and when in pain or distress, from information gathered proactively with involvement from family and informal carers. It shows how other health professionals, and the patient's family, can use this to ensure improved diagnosis and treatment for people who can't effectively communicate when they are in pain.

17. Meng Jing, Li Zuoshan, Shen Lin. **Altered neuronal habituation to hearing others' pain in adults with autistic traits**. *Scientific Reports*. 2020; **10**(1).

This study tested the hypothesis that autistic traits influence the neuronal habituation that underlies the processing of others' pain. Based on their autism-spectrum quotient (AQ), two groups of participants were classified according to their autistic traits: High-AQ and Low-AQ groups. Their event-related potentials in response to trains of three identical audio recordings, exhibiting either painful or neutral feelings of others, were compared during three experimental tasks. (1) In a Pain Judgment Task, participants were instructed to focus on pain-related cues in the presented audio recordings. (2) In a Gender Judgment Task, participants were instructed to focus on non-pain-related cues in the presented audio recordings. (3) In a Passive Listening Task, participants were instructed to passively listen. In the High-AQ group, an altered empathic pattern of habituation, indexed by frontal-central P2 responses of the second repeated painful audio recordings, was found during the Passive Listening Task. Nevertheless, both High-AQ and Low-AQ groups exhibited similar patterns of habituation to hearing others' voices, both neutral and painful, in the Pain Judgment and Gender Judgment Tasks. These results suggest altered empathic neuronal habituation in the passive processing of others' vocal pain by individuals with autistic traits.

18. Kornblau Barbara, Robertson Scott, Mbiza Sarah, Mottley Saint-Claire, Clark Heaven, Lang Kahler, Alexander Aurelia. **Autism and Pain: How Autistic Adults Perceive Pain...2020 AOTA Annual Conference & Expo**. *American Journal of Occupational Therapy*. 2020; **74**(Sup1): 1-.

Date Presented 03/27/20 This qualitative study explored perceptions of pain by autistic adults through an online survey of open-ended questions via Qualtrics. Autistic adults were recruited from four Internet support communities. Qualitative data was analyzed using grounded theory coding methods until saturation was reached. Multiple researchers and data from

multiple sources ensured rigor, trustworthiness, and triangulation. This study provides pain-perception consideration for the treatment of autistic adults. Primary Author and Speaker: Barbara Kornblau Additional Authors and Speakers: Aurelia Alexander Contributing Authors: Scott Robertson, Sarah Mbiza, Saint-Claire Mottley, Heaven Clark, Kahler Lang

19. Failla Michelle D., Gerdes Madison B., Williams Zachary J., Moore David J., Cascio Carissa J. **Increased pain sensitivity and pain-related anxiety in individuals with autism**. *Pain reports*. 2020; **5**(6): e861.

Introduction: Individuals with autism spectrum disorder (ASD) often exhibit differences in pain responsivity. This altered responsivity could be related to ASD-related social communication difficulties, sensory differences, or altered processing of pain stimuli. Previous neuroimaging work suggests altered pain evaluation could contribute to pain-related anxiety in ASD.; Objectives: We hypothesized that individuals with ASD would report increased pain sensitivity and endorse more pain-related anxiety, compared to typically developing controls.; Methods: We recruited 43 adults (ASD, n = 24; typically developing, n = 19) for 3 heat pain tasks (applied to the calf). We measured heat pain thresholds using a method of limits approach, a pain-rating curve (7 temperatures between 40 and 48°C, 5 seconds, 5 trials each), and a sustained heat pain task with alternating low (42°C) and high (46°C) temperatures (21 seconds, 6 trials each). Individual differences in pain-related anxiety, fear of pain, situational pain catastrophizing, depressive symptoms, and autism-related social communication were assessed by self-report.; Results: There were no group differences in pain thresholds. For suprathreshold tasks, mean pain ratings were higher in ASD across both the pain-rating curve and the sustained heat pain tasks, but responses in the ASD group were more varied. Pain anxiety (PASS-Total) and pain-related fear (FOP-III-Total) were higher in the ASD group and were positively associated with pain ratings.; Conclusions: Our results suggest that both sensory and cognitive experiences of pain are heightened and interact reciprocally in adults with ASD. Future studies are needed to evaluate the impact of pain-related anxiety on treatment-seeking and pain behaviors, given higher levels of pain-related anxiety in ASD.

20. Dubois A., Boudjarane M., Le Fur-Bonnabesse A., Dion A., L'Heveder G., Quinio B., Walter M., Marchand S., Bodéré C. **Pain modulation mechanisms in ASD adults**. *Journal of Autism and Developmental Disorders*. 2020; **50**(8): 2931-40.

We tested endogenous pain modulation mechanisms in adults with autism spectrum disorders (ASD). Nineteen ASD adults without intellectual disabilities were included, matched with 19 healthy volunteers on the basis of sex and chronological age. An experimental pain model was used to measure excitatory and inhibitory pain mechanisms in a single session. Statistical analyses indicated that endogenous pain modulation mechanisms in ASD group did not differ significantly from those of healthy adults. The pain scores were very disparate in ASD group with a greater range of extreme scores than in control group. Unlike schizophrenic patients, there was no systematic dysfunction of endogenous excitatory pain modulation mechanisms, but the high variability requires to be wise to interpret the results and formulate conclusion

21. Defaye Manon, Gervason Sandie, Altier Christophe, Berthon Jean-Yves, Ardid Denis, Filaire Edith, Carvalho Frédéric Antonio. **Microbiota: A novel regulator of pain**. *Journal of Neural Transmission*. 2020; **127**(4): 445-65.

Among the various regulators of the nervous system, the gut microbiota has been recently described to have the potential to modulate neuronal cells activation. While bacteria-derived products can induce aversive responses and influence pain perception, recent work suggests that 'abnormal' microbiota is associated with neurological diseases such as Alzheimer's, Parkinson's disease or autism spectrum disorder (ASD). Here we review how the gut microbiota modulates afferent sensory neurons function and pain, highlighting the role of the microbiota/gut/brain axis in the control of behaviors and neurological diseases. We outline the changes in gut microbiota, known as dysbiosis, and their influence on painful gastrointestinal disorders. Furthermore, both direct host/microbiota interaction that implicates activation of 'pain-sensing' neurons by metabolites, or indirect communication via immune activation is discussed. Finally, treatment options targeting the gut microbiota, including pre- or probiotics, will be proposed. Further studies on microbiota/nervous system interaction should lead to the identification of novel microbial ligands and host receptor-targeted drugs, which could ultimately improve chronic pain management and well-being.

22. Brown Chad O., Uy Jarryll, Singh Karun K. **A mini-review: Bridging the gap between autism spectrum disorder and pain comorbidities**. *Canadian journal of pain = Revue canadienne de la douleur*. 2020; **4**(4): 37-44.

Background: Pain is a complex neurobiological response with a multitude of causes; however, patients with autism spectrum disorder (ASD) often report chronic pain with no known etiology. Recent research has been aimed toward identifying the causal mechanisms of pain in mouse and human models of ASD. In recent years, efforts have been made to better document and explore secondary phenotypes observed in ASD patients in the clinic. As new sequencing studies have become more powered with larger cohorts within ASD, specific genes and their variants are often left uncharacterized or validated. In this review we highlight ASD risk genes often presented with pain comorbidities.; Aims: This mini-review bridges the gap between two fields of literature, neurodevelopmental disorders and pain research. We discuss the importance of the genetic landscape of ASD and its links to pain phenotypes.; Results: Among the numerous genes implicated in ASD, few have been implicated with varying severities of pain comorbidity. Mutations in these genes, such as SCN9A, SHANK3 , and CNTNAP2 , lead to altered neuronal function that produce different responses to pain, shown in both mouse and human models.; Conclusion: There is a necessity to use new technologies to advance the current understanding of ASD risk genes and their contributions to pain. Secondly, there is a need to power future ASD risk genes associated with pain with their own cohort, because a better understanding is needed of this subpopulation.

23. Whitney Daniel G., Shapiro Danielle N. **National Prevalence of Pain Among Children and Adolescents With Autism Spectrum Disorders**. *JAMA pediatrics*. 2019; **173**(12): 1203-5.

24. Vaughan Sarah, Failla Michelle D., Poole Helen M., Forshaw Mark J., McGlone Francis, Cascio Carissa J., Moore David J. **Pain processing in psychiatric conditions: A systematic review**. *Review of General Psychology*. 2019; **23**(3): 336-58.

Pain is a universal, multidimensional experience with sensory, emotional, cognitive, and social components, which is fundamental to our environmental learning when functioning typically. Understanding pain processing in psychiatric conditions could provide unique insight into the underlying pathophysiology or psychiatric disease, especially given the psychobiological overlap with pain processing pathways. Studying pain in psychiatric conditions is likely to provide important insights, yet, there is a limited understanding beyond the work in depression and anxiety. This is a missed opportunity to describe psychiatric conditions in terms of neurobiological alterations. To examine the research into the pain experiences of these groups and the extent to which a-typicality is present, a systematic review was conducted. An electronic search strategy was developed and conducted in several databases. The current systematic review included 46 studies covering five Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5) disorders: autism, attention-deficit hyperactivity disorder (ADHD), schizophrenia, personality disorder, and eating disorders, confirming tentative evidence of altered pain and touch processing. Specifically, hyposensitivity is reported in schizophrenia, personality disorder and eating disorder, hypersensitivity in ADHD, and mixed results for autism. Review of the research highlights a degree of methodological inconsistency in the utilization of comprehensive protocols, the lack of which fails to allow us to understand whether a-typicality is systemic or modality specific.

25. Seegers Hélène, Serani Isabelle, Bogar Mireille, Gei Maria, Baudet Véronique, Witz Laetitia, Bouchard Jean-Pierre. **L'approche Snoezelen dans la prise en charge de la douleur en psychiatrie**. *Soins Psychiatrie*. 2019; **40**(320): 35-40.

The approach or practice known as Snoezelen is defined as the controlled multi-sensory stimulation of a person's sensoriality in a safe space. It has recognised benefits in the management of severe mental health disabilities. But, can it have a more specific benefit in psychiatry in terms of pain managment? Hospital caregivers go some way to answering the question by sharing their thoughts and experience regarding an innovative clinical experiment using the Snoezelen approach for this purpose. (Copyright © 2018. Published by Elsevier Masson SAS.)

26. Penmetsa Chandana, Penmetcha Sarada, Cheruku Sampath Reddy, Mallineni Sreekanth Kumar, Patil Anil Kumar, Namineni Srinivas. **Role of Dental Discomfort Questionnaire-Based Approach in Recognition of Symptomatic Expressions Due to Dental Pain in Children with Autism Spectrum Disorders**. *Contemporary clinical dentistry*. 2019; **10**(3): 446-51.

Aim: The aim of this study is to investigate whether the Dental Discomfort Questionnaire (DDQ) could help to identify toothaches in children with autism spectrum disorder (ASD).; Materials and Methods: This study involved sixty children between the age groups of 6-16 years, attending the day-care schools diagnosed with ASD. Five different groups of children were identified based on the presence of a toothache and/or carious teeth. The DDQ-8 was completed by parents and evaluated by a single examiner. Data were analyzed using descriptive statistics (SPSS version 17), and a correlation was observed between the total DDQ

score and the decayed, missing, and filled teeth (dmft-DMFT) score.; Results: Analysis of the data showed that DDQ-8 had a significant correlation with that of DMFT score in a group "with carious teeth but no toothache" (r = 0.497, P = 0.019) and group "with carious teeth and a toothache" (r = 0.682 P = 0.043). A group "without carious teeth where the parents were not sure whether or not the child had a toothache" had higher mean compared to other groups with DDQ-8 scores.; Conclusion: There was a significant difference in the total mean DDQ scores when they were compared with that of the control group. Children with high DDQ-8 often had a high DMFT/dmft score. A significant correlation was found when the total DDQ-8 scores were compared with that of the DMFT score.

27. Meng Jing, Shen Lin, Li Zuoshan, Peng Weiwei. **Top-down Effects on Empathy for Pain in Adults with Autistic Traits**. *Scientific Reports*. 2019; **9**(1): 1-13.

While empathic responses of individuals with autism-spectrum disorder have been reported to be modulated by top-down attention, it remains unclear whether empathy for pain in typically developing individuals with autistic traits also involves such top-down modulation mechanisms. This study employed the autism-spectrum quotient (AQ) to quantify autistic traits in a group of 1,231 healthy adults. Two subset groups (High-AQ and Low-AQ groups) were randomly selected from the highest and lowest 10% AQ scores respectively. We explored whether participants in both groups would differ in their response to others' pain when their attention was directed toward (A-P tasks) or away (A-N tasks) from pain cues in auditory and visual experimental modalities. Compared to Low-AQ individuals, High-AQ individuals exhibited more suppressed N1 and P2 amplitudes in response to painful vocal cues in auditory A-N tasks. This suggests suppressed attentional and emotional processes of empathy for pain when High-AQ individuals have their attention directed away from others' pain cues. No significant difference was found between both groups in the auditory A-P task, nor in the visual A-P and A-N tasks. These results suggest that top-down attention modulation of cortical empathic responses to others' vocal pain is influenced by autistic traits.

28. Li Bi Lian, Yuen Vivian Man-ying, Zhang Na, Zhang Huan Huan, Huang Jun Xiang, Yang Si Yuan, Miller Jeffery W., Song Xing Rong. **A comparison of intranasal dexmedetomidine and dexmedetomidine plus buccal midazolam for non-painful procedural sedation in children with autism**. *Journal of Autism and Developmental Disorders*. 2019; **49**(9): 3798-806.

Children with autism often need sedation for diagnostic procedures and they are often difficult to sedate. This prospective randomized double-blind control trial evaluates the efficacy and safety using intranasal dexmedetomidine with and without buccal midazolam for sedation in children with autism undergoing computerized tomography and/or auditory brainstem response test. The primary outcome is the proportion of children attaining satisfactory sedation. One hundred and thirty-six children received intranasal dexmedetomidine and 139 received intranasal dexmedetomidine with buccal midazolam for sedation. Combination of intranasal dexmedetomidine and buccal midazolam was associated with higher sedation success when compared to intranasal dexmedetomidine. Since intranasal and buccal sedatives required little cooperation this could be especially useful technique for children with autism or other behavioral conditions.

29. Garcia-Villamisar D., Moore D., Garcia-Martínez M. **Internalizing symptoms mediate the relation between acute pain and autism in adults**. *Journal of Autism and Developmental Disorders*. 2019; **49**(1): 270-8.

Research on pain in autism spectrum disorder (ASD) is in its infancy, with almost nothing known about how individual differences may predicting pain response in ASD. In the present study, 45 adults (28 male, age 22–48 years) with diagnoses of autism and intellectual delay were observed during vaccination or dental cleaning and their pain behaviours coded and measures of autism symptom severity, anxiety, depression and obsessivity taken. Our findings showed that greater autism severity predicted greater pain response which was partially mediated by anxiety and depression. These data suggest that mental health symptoms are important when considering pain response in autism. Mood must therefore be considered in future research on pain in ASD as well as clinical pain management.

30. Failla M., Davis S., Gerdes M., Williams Z., Moore D., Cascio C. **(262) Increased Heat Pain Sensitivity and Pain-Related Anxiety in Individuals with Autism**. *Journal of Pain*. 2019; **20**: S40-S.

31. Cappuccio Gerarda, Bernardo Pia, Raiano Enza, Pinelli Michele, Alagia Marianna, Esposito Marcello, Della Casa Roberto, Strisciuglio Pietro, Brunetti-Pierri Nicola, Bravaccio Carmela, Brunetti-Pierri Nicola. **Pain and sleep disturbances in Rett syndrome and other neurodevelopmental disorders**. *Acta Paediatrica*. 2019; **108**(1): 171-2.

A Medical report is present on Pain and sleep disturbances in Rett syndrome and other neurodevelopmental disorders. The article mention about the Rett syndrome as a severe neurodevelopmental disorder, mostly caused by a MECP2 gene mutation, with some overlaps with autism spectrum disorders and cerebral palsy; and effects of Rett syndrome such as scoliosis, constipation, gastrointestinal problems and self-injuries.

32. Asztély Karin, Kopp Svenny, Gillberg Christopher, Waern Margda, Bergman Stefan. **Chronic Pain And Health-Related Quality Of Life In Women With Autism And/Or ADHD: A Prospective Longitudinal Study**. *Journal of pain research*. 2019; **12**: 2925-32.

Purpose: To investigate the prevalence of chronic pain and its association with health-related quality of life (HRQoL) in a group of women, diagnosed with autism spectrum disorder (ASD) and/or attention deficit hyperactive disorder (ADHD) in childhood.; Patients and Methods: Prospective longitudinal 16-19 years follow-up study of 100 Swedish females diagnosed with ASD and/or ADHD in childhood/adolescence. Seventy-seven of the women were included in the current sub-study, using validated measures of pain perception and quality of life.; Results: A large majority of the women (76.6%) reported chronic pain. HRQoL was low overall and lower still for those reporting chronic pain. Women with ADHD who had ongoing treatment with stimulants reported a significant lower prevalence of chronic widespread pain (CWP) than those not treated.; Conclusion: Comorbidity with chronic pain is common in women with ASD and/or ADHD and important to address in the clinic since it is associated with an already low HRQoL. Treatment for ADHD might reduce the pain in some cases.