



# MATRICS

NEWSLETTER 1 - SUMMER 2016

## MATRICS launches Newsletter

Welcome to the first MATRICS newsletter!

MATRICS is a multidisciplinary consortium of academic partners and small and medium-sized enterprises (SMEs) that focuses on the subtyping of aggression both within disruptive behavior disorder (DBD) and of the broader cross-disorder trait of aggression.

The newsletter has been established and will be edited mainly by the MATRICS Junior Group. Its aim is to use the extensive knowledge and expertise within our consortium to inform a broader public about our research. With this medium, we hope to give patients and relatives a better insight into the progress of this project, but also into the people working passionately to better understand aggressive behavior. We further aim to inform fellow researchers interested in aggressive behavior about upcoming conferences and interesting recent publications.

The newsletter is scheduled to appear 2-3 times per year. Each issue will comprise a News section, recent publications, as well



MATRICS Kickoff Meeting 2014

as information on upcoming meetings and conferences. Further, within each issue one of our collaborating institutions will be introduced, and short Q&A interviews with one junior member of the consortium will be included. Q&A interviews with one senior member will be added starting with the second newsletter.

For feedback about the newsletter or questions regarding the MATRICS project please contact [info@matrics-project.eu](mailto:info@matrics-project.eu)

Best wishes,  
The Editorial Team

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# News: Meetings and Events

TEXT: CHRISTIANA LABERMAIER

## MATRICS 2<sup>nd</sup> General Assembly

The 2<sup>nd</sup> General Assembly took place in Rome on March 29<sup>th</sup> – 31<sup>st</sup> 2015 and was attended by representatives of all MATRICS partners, members of the Scientific and Ethical Advisory Board, as well as invited guest speakers (Dr. Inti Brazil, Prof. Caroline Blanchard, Prof. Antonio Persico and Dr. James Blair).



MATRICS General Assembly Rome

## MATRICS Steering Committee Meeting

The Steering Committee meets twice a year: once on the occasion of General Assembly meetings, and once more after six months to review the project's progress. The 4<sup>th</sup> SC meeting was held in Lisbon. The next SC Meeting is scheduled for October 19<sup>th</sup> – 20<sup>th</sup> and will be held in Berlin, Germany



MATRICS Steering Committee Meeting Lisbon



## MATRICS 3<sup>rd</sup> General Assembly

The General Assembly meets once a year to present and discuss the results that have been achieved so far, and to determine and discuss the next steps within the MATRICS project. The last meeting was held in Mallorca on April 14<sup>th</sup> – 16<sup>th</sup> 2016 and was attended by representatives of all MATRICS partners, as well as Dr. Luna Centifanti as an invited guest speaker.

## EFCAP Symposium in Porto

We are happy to announce that the MATRICS project was represented with 2 symposia (*"Towards a translational approach of disruptive behavior disorders?"* and *"Multidisciplinary therapeutic and institutional approaches for adolescents with disruptive behavior disorders"*) at the 5th EFCAP congress in Porto this year. The meeting's main focus was the mental health needs of young offenders and victims. The congress provided new insight into assessment procedures, intervention strategies and programs and legal issues related to mental health problems of both young offenders and victims. The MATRICS project is fitting extremely well into this year's program and furthermore enabled us to disseminate our findings within the scientific community.



# News: The Junior Scientists Group

TEXT: AMANDA JAGER & SARAH BAUMEISTER

We are happy to announce that our MATRICS Consortium has its own Junior Scientist Group. Officially founded in March 2015, during the second general assembly meeting in Rome, the aims of this group are to foster the career development as well as translational exchange and collaboration within the young, talented researchers working in the consortium.

To this end, a framework of support has been established and will be extended over the course of the MATRICS project. Within this framework, selected senior scientists are invited to participate in internal workshops during the Junior Scientist Group meetings. During the first Junior Group meeting in Rome, Dr. Inti A. Brazil, Prof. Caroline Blanchard and Dr. Geert Poelmans were invited to give advises on career related issues. Prof. Caroline Blanchard, a female role model for women in science, was specifically invited to talk about how to develop a well-recognized career in a sometimes man dominated world.



The second MATRICS Junior Group Meeting took place in April 2016 in Mallorca. Dr. Luna Centifanti was the guest scientist for this meeting, who shared her personal career development experiences. Dr. Centifanti as well as Dr. Geert Poelmans and Dr. Jeffrey Glennon were further approachable for all junior scientists throughout the meeting for career and scientific advice.

To extend the framework of support, an autumn school is currently planned in collaboration with the aggression-related projects Aggrosotype and ACTION, where junior scientists will get the chance to participate and take part in workshops and courses.

Finally, the MATRICS newsletter has been established and will be curated mainly by the Junior Group. The aim of this newsletter is to use the extensive knowledge and expertise within our consortium to inform a broader public about our research. Since the juniors will do most of the practical work within MATRICS, we hope to give patients and relatives a better insight into the progress of this project. Please do not hesitate to contact MATRICS if you have any questions about our project and Junior's program.



1<sup>st</sup> Junior Group Meeting from left to right: Alessio Squassina, Francesca Zoratto, Inti Brazil, Amanda Jager, Peter Zijderveld, Geert Poelmans, Jeffrey Glennon, Mireille Bakker, Kate Lievesley, Sara Carucci, Sarah Baumeister, Kate Warre-Cornish, Damien Huzard, Alireza Abaei, Chiara Spinello and Danilo Ingiosi

# Lab Visit: Central Institute for Mental Health Mannheim: Developmental Clinical Neurophysiology

## Who works in your lab?

The interdisciplinary team of the Department of Child and Adolescent Psychiatry and Psychotherapy (Director: Tobias Banaschewski) comprises a research staff of 38 people. Within this framework, our research group, led by Dani Brandeis, consists of 5 postdocs (4 Psychologists, 1 Psychiatrist), 2 PhD students (both Psychologists) and 3 research assistants.



Developmental Clinical Neurophysiology:  
Aggression research team

## What kind of research do you do?

Our research group focuses on multimodal brain imaging and neurophysiology like EEG-fMRI in children and adolescents during development, in psychiatric disorders or risks due to gene-environment interactions, and concentrates on potential neurobiological markers of disorders such as ADHD, Autism, OCD and Aggression in ODD/CD for subtyping and predicting treatment response. A translational focus of our group is research on neuro-and biofeedback treatment addressing clinical relevance and treatment-induced neuronal plasticity.

## What is your favorite or most used equipment / technique / software?

Our by far most used software is Matlab with SPM for fMRI data analysis, followed by the Brain Vision Analyzer for EEG and skin conductance data and SPSS for overall data analysis. Our MRI scanner and our EEG systems and skin conductance electrodes are our most used equipment.

## What is the best part about your lab?

Our lab is very well embedded in the Central Institute for Mental Health Mannheim, with a lot of expertise, good infrastructure and excellent scientific exchange. Within our research group we have a pleasant working environment with very friendly relations.

## What makes your lab special? Share a quirky fact about your group!

In our research group we are very good at celebrating birthdays. We always have a minimum of 2 different homemade cakes and really take time to sit down and enjoy the coffee and cake together.

## What was your lab's biggest success in the last year?

We were able to get funding for a project on predicting treatment response from brain structure and function for evidence based stepped care of ADHD. Further, three of our PhD students graduated.

# Meet the Junior: Damien Huzard

EPFL LAUSANNE, LABORATORY OF BEHAVIORAL GENETICS IN THE BRAIN  
MIND INSTITUTE

## What is your current position?

I am a 3<sup>rd</sup> year PhD student.

## What are your main research interests?

I am working on preclinical models displaying abnormal aggressive behaviors. I am currently studying the effects of stress and stress reactivity on social behaviors as well as the links with the autonomic nervous system regulation in basal conditions and during stress experiences. The goal is to study early-life stress and early-life stress-reactivity programming leading to increased aggressivity and decreased sociability in order to determine the brain regions and neuromodulators involved in the abnormal behaviors observed. Knowing the cross-talk between the stress system and the autonomic nervous system, I am currently analyzing more in details the heart-rate variability of rats in order to target specific systems that may be altered after early life experiences.

## The first thing you do when you get to the office / lab?

Drink a tea, check my emails and my experimental planning of the day.

## What was your biggest success?

I think that I am still too young to have a big success I could be proud of all my life, but scientifically speaking, writing my first article after my Master's project was a huge step into the world of science that taught me a lot and validated my interest in a scientific career. Indeed, it showed me that I was able to run a complete experiment, from the design to the publication, going through all the different steps and issues and managing to deal with those in order to publish it.

## What makes you show your aggressive side?

I am against violence in general and I think that, as occidental humans leaving in 2016, we can most of the time manage to deal with issues in more intelligent ways than by using aggression. But we live in a society that leads to more inequalities and abuses of authority which make me feel uncomfortable and angry.



## Describe your career path so far.

I am French but I moved to Switzerland after my Baccalauréat and I did my Bachelor and Master's at EPFL in Lausanne with main focuses on Life Sciences and a specialization on Neurosciences during the Master. I spent 8 months in Concordia University in Montreal for my Master's thesis. I was studying the effects of enriched environments on animals submitted to stress.

## Coffee, chocolate, sports? What is your "doping"?

No coffee, but loads of tea! And even if I live in Switzerland, I am not so much a chocolate eater... But I do a lot of bouldering which is a climbing style without ropes and below 3-4 meters. In bouldering, I like the fact that to solve a "problem" you need to combine strength, balance, logic, tonicity and flexibility. It is a complete sport that is both physically and mentally stimulating and challenging.



# Newsflash: Recent publications

## RECENT PUBLICATIONS FROM THE MATRICS CONSORTIUM

**TITLE:** Neuroligin-2 expression in the prefrontal cortex is involved in attention deficits induced by peripubertal stress.

**AUTHORS:** Tzanoulinou, S., Garcia-Mompo, C., Riccio, O., Grosse, J., Zanoletti, O., Dedousis, P., Nacher, J., Sandi, C.

**JOURNAL, YEAR:** Neuropsychopharmacology, 2016, 41(3):751-761.

Emerging evidence indicates that attention deficits, which are frequently observed as core symptoms of neuropsychiatric disorders, may be elicited by early life stress. The prefrontal cortex (PFC) has been implicated in the regulation of attention, including dysfunctions in GABAergic transmission, and it is highly sensitive to stress. This Study investigated the involvement of neuroligin-2 (NLGN-2), a synaptic cell adhesion molecule involved in the stabilization and maturation of GABAergic synapses, in the PFC in the link between stress and attention deficits. First, the authors established that exposure of rats to stress during the peripubertal period impairs attention in the five-choice serial reaction time task and results in reductions in the GABA-synthesizing enzyme glutamic acid decarboxylase in different PFC subregions (ie, prelimbic (PL), infralimbic, and medial and ventral orbitofrontal (OFC) cortex) and in NLGN-2 in the PL cortex. In peripubertally stressed animals, NLGN-2 expression in the PL and OFC cortex correlated with attention measurements. Subsequently, they found that adeno-associated virus-induced rescue of NLGN-2 in the PFC reverses the stress-induced attention deficits regarding omitted trials. Therefore, their findings highlight peripuberty as a period that is highly vulnerable to stress, leading to the development of attention deficits and a dysfunction in the PFC GABAergic system and NLGN-2 expression.

**TITLE:** The Programming of the Social Brain by Stress During Childhood and Adolescence: From Rodents to Humans.

**AUTHORS:** Tzanoulinou, S. & Sandi, C.

**JOURNAL, YEAR:** Current topics in behavioral neurosciences, 2016.

The quality and quantity of social experience is fundamental to an individual's health and well-being. Early life stress is known to be an important factor in the programming of the social brain that exerts detrimental effects on social behaviors. The peri-adolescent period, comprising late childhood and adolescence, represents a critical developmental window with regard to the programming effects of stress on the social brain. Here, the authors discuss social behavior and the physiological and neurobiological consequences of stress during peri-adolescence in the context of rodent paradigms that model human adversity, including social neglect and isolation, social abuse, and exposure to fearful experiences. Furthermore, they discuss peri-adolescent stress as a potent component that influences the social behaviors of individuals in close contact with stressed individuals and that can also influence future generations. The authors also discuss the temporal dynamics programmed by stress on the social brain and debate whether social behavior alterations are adaptive or maladaptive. By revising the existing literature and defining open questions, they aim to expand the framework in which interactions among peri-adolescent stress, the social brain, and behavior can be better conceptualized.

# Newsflash: Recent publications

## RECENT PUBLICATIONS FROM THE MATRICS CONSORTIUM

**TITLE:** The effects of stress during early postnatal periods on behavior and hippocampal neuroplasticity markers in adult male mice.

**AUTHORS:** van der Kooij, M.A., Grosse, J., Zanoletti, O., Papilloud, A., Sandi, C.

**JOURNAL, YEAR:** Neuroscience, 2016, 311:508-518.

Infancy is a critical period for brain development. Disrupted maternal care is known to interfere with neurodevelopmental processes and may lead to the manifestation of behavioral abnormalities in adulthood. Mouse dams confronted with insufficient bedding/nesting material have been shown to provide fragmented maternal care to their offspring. The authors compared the impact of this model of early-life stress (ELS) during different developmental periods comprising either postnatal days (PNDs) 2–9 (ELS-early) or PND 10–17 (ELS-late) on behavior and hippocampal cell adhesion molecules in male mice in adulthood. ELS-early treatment caused a permanent reduction in bodyweight, whereas this reduction only occurred transiently during juvenility in ELS-late mice. Anxiety was only affected in ELS-late mice, while cognition and sociability were equally impaired in both ELS-treated groups. They further analyzed hippocampal gene expression of the  $\gamma 2$  subunit of the GABA<sub>A</sub> receptor (Gabrg2) and of genes encoding cell adhesion molecules. Gabrg2 expression was increased in the ventral hippocampus in ELS-late-treated animals and was correlated with anxiety-like behavior in the open-field (OF) test. ELS-early-treated animals exhibited an increase in nectin-1 expression in the dorsal hippocampus, and this increase was associated with the social deficits seen in these animals.

**TITLE:** Genetics of aggressive behavior: An overview.

**AUTHORS:** Veroude, K., Zhang-James, Y., Fernández-Castillo, N., Bakker, M.J., Cormand, B., Faraone, S.V.

**JOURNAL, YEAR:** American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 2016, 171:3-34

The Research Domain Criteria (RDoC) address three types of aggression: frustrative non-reward, defensive aggression and offensive/proactive aggression. This review sought to present the evidence for genetic underpinnings of aggression and to determine to what degree prior studies have examined phenotypes that fit into the RDoC framework. Twin studies show that about half the variance in behavior may be explained by genetic risk factors. This is true for both dimensional, trait-like, measures of aggression and categorical definitions of psychopathology. The non-shared environment seems to have a moderate influence with the effects of shared environment being unclear. Human molecular genetic studies of aggression are in an early stage. The most promising candidates are in the dopaminergic and serotonergic systems along with hormonal regulators. Genome-wide association studies have not yet achieved genome-wide significance, but current samples are too small to detect variants having small effects. The strongest molecular evidence for a genetic basis for aggression comes from animal models comparing aggressive and non-aggressive strains or documenting the effects of gene knockouts. Although we have learned much from these prior studies, future studies should improve the measurement of aggression by using a systematic method of measurement such as that proposed by the RDoC.

# Newsflash: Recent publications

## RECENT PUBLICATIONS FROM THE MATRICS CONSORTIUM

**TITLE:** The poor outcome of conduct disorders: a need for innovative, more effective therapeutic interventions

**AUTHORS:** Zuddas, A.

**JOURNAL, YEAR:** European Child & Adolescent Psychiatry, July 2014, 23: 515-517

Conduct disorder (CD) is defined as a repetitive and persistent pattern of behaviour, which violates the rights of others and major age-appropriate societal rules. A study of Kretschmer et al. using a sophisticated statistical approach, including latent class growth analysis and a set of logistic regression models, the authors identified four developmental trajectories [“low”, “childhood limited” (CL), “early onset persistent” (EOP) and “adolescent onset” (AO)]. Individuals who displayed EOP were at greater risk for a large series of adulthood problems ranging from alcohol, tobacco, cannabis and other drug use to criminal offenses, self-harm, gambling, risky sexual behaviour to anxiety and depression. The EOP class was three times more likely than the “low” class to consume cannabis, and twice as likely to engage in smoking and risky sexual behaviour (results also observed for the AO class). The programmes AGGRESSOTYPE & MATRICS will each include nested projects, finalized to identify neural, genetic and molecular factors involved in the pathogenesis of aggression/antisocial behaviour in preclinical (animal) models and clinical samples, in order to develop and pilot-test preventive interventions in very young children at very high risk and to perform proof-of-concept clinical studies in order to identify innovative pharmacological interventions.

**TITLE:** Neuropsychosocial profiles of current and future adolescent alcohol misusers

**AUTHORS:** Whelan, R. et al.

**JOURNAL, YEAR:** Nature, 2014, 512: 185-189

Animal models can demonstrate the effects of neurotoxic substances; however, they provide limited insight into the psycho-social and higher cognitive factors involved in the initiation of substance use and progression to misuse. One can search for pre-existing risk factors by testing for endophenotypic biomarkers in non-using relatives; however, these relatives may have personality or neural resilience factors that protect them from developing dependence. A longitudinal study has potential to identify predictors of adolescent substance misuse, particularly if it can incorporate a wide range of potential causal factors, both proximal and distal, and their influence on numerous social, psychological and biological mechanisms. Here they apply machine learning to a wide range of data from a large sample of adolescents (n = 692) to generate models of current and future adolescent alcohol misuse that incorporate brain structure and function, individual personality and cognitive differences, environmental factors (including gestational cigarette and alcohol exposure), life experiences, and candidate genes. These models were accurate and generalized to novel data, and point to life experiences, neurobiological differences and personality as important antecedents of binge drinking. By identifying the vulnerability factors underlying individual differences in alcohol misuse, these models shed light on the aetiology of alcohol misuse and suggest targets for prevention.



# Newsflash: Recent publications

## RECENT PUBLICATIONS FROM THE MATRICS CONSORTIUM

**TITLE:** Robust regression for large-scale neuroimaging studies

**AUTHORS:** Fritsch, V. et al.

**JOURNAL, YEAR:** Neurolmage, 2015, 111: 431-441

While studies with small sample sizes can rarely be shown to deviate from standard hypotheses (such as the normality of the residuals) due to the poor sensitivity of normality tests with low degrees of freedom, large-scale studies (e.g. > 100 subjects) exhibit more obvious deviations from these hypotheses and call for more refined models for statistical inference. Here, the authors demonstrate the benefits of robust regression as a tool for analyzing large neuroimaging cohorts. First, they use an analytic test based on robust parameter estimates; based on simulations, this procedure is shown to provide an accurate statistical control without resorting to permutations. Second, they show that robust regression yields more detections than standard algorithms using as an example an imaging genetics study with 392 subjects. Third, the authors show that robust regression can avoid false positives in a large-scale analysis of brain-behavior relationships with over 1500 subjects. Finally they embed robust regression in the Randomized Parcellation Based Inference (RPBI) method and demonstrate that this combination further improves the sensitivity of tests carried out across the whole brain. Altogether, their results show that robust procedures provide important advantages in large-scale neuroimaging group studies.

**TITLE:** Cannabis use in early adolescence: Evidence of amygdala hypersensitivity to signals of threat

**AUTHORS:** Spechler, P.A. et al.

**JOURNAL, YEAR:** Developmental Cognitive Neuroscience, 2015, 16: 63-70

Cannabis use in adolescence may be characterized by differences in the neural basis of affective processing. In this study, the authors used an fMRI affective face processing task to compare a large group ( $n = 70$ ) of 14-year olds with a history of cannabis use to a group ( $n = 70$ ) of never-using controls matched on numerous characteristics including IQ, SES, alcohol and cigarette use. The task contained short movies displaying angry and neutral faces. Results indicated that cannabis users had greater reactivity in the bilateral amygdalae to angry faces than neutral faces, an effect that was not observed in their abstinent peers. In contrast, activity levels in the cannabis users in cortical areas including the right temporal-parietal junction and bilateral dorsolateral prefrontal cortex did not discriminate between the two face conditions, but did differ in controls. Results did not change after excluding subjects with any psychiatric symptomology. Given the high density of cannabinoid receptors in the amygdala, the findings suggest cannabis use in early adolescence is associated with hypersensitivity to signals of threat. Hypersensitivity to negative affect in adolescence may place the subject at-risk for mood disorders in adulthood.

# Newsflash: Recent publications

## RECENT PUBLICATIONS FROM THE MATRICS CONSORTIUM

**TITLE:** Common genetic variants influence human subcortical brain structures

**AUTHORS:** Hibar, D.P. et al.

**JOURNAL, YEAR:** Nature, 2015, 520: 224-229

The structure of the human brain is strongly shaped by genetic influences. Subcortical brain regions form circuits with cortical areas to coordinate movement, learning, memory and motivation, and altered circuits can lead to abnormal behaviour and disease. To investigate how common genetic variants affect the structure of these brain regions, the authors conduct genome-wide association studies of the volumes of seven subcortical regions and the intracranial volume derived from magnetic resonance images of 30,717 individuals from 50 cohorts. They identify five novel genetic variants influencing the volumes of the putamen and caudate nucleus. They also find stronger evidence for three loci with previously established influences on hippocampal volume and intracranial volume. These variants show specific volumetric effects on brain structures rather than global effects across structures. The strongest effects were found for the putamen, where a novel intergenic locus with replicable influence on volume (rs945270;  $P = 1.08 \times 10^{-33}$ ; 0.52% variance explained) showed evidence of altering the expression of the KTN1 gene in both brain and blood tissue. Variants influencing putamen volume clustered near developmental genes that regulate apoptosis, axon guidance and vesicle transport. Identification of these genetic variants provides insight into the causes of variability in human brain development, and may help to determine mechanisms of neuropsychiatric dysfunction.

**TITLE:** Association of Protein Phosphatase PPM1G With Alcohol Use Disorder and Brain Activity During Behavioral Control in a Genome-Wide Methylation Analysis

**AUTHORS:** Ruggeri, B. et al.

**JOURNAL, YEAR:** American Journal of Psychiatry, 2015, 72: 543-552

The genetic component of alcohol use disorder is substantial, but monozygotic twin discordance indicates a role for nonheritable differences that could be mediated by epigenetics. Despite growing evidence associating epi-genetics and psychiatric disorders, it is unclear how epi-genetics, particularly DNA methylation, relate to brain function and behavior, including drinking behavior.

The authors carried out a genome-wide analysis of DNA methylation of 18 monozygotic twin pairs discordant for alcohol use disorder and validated differentially methylated regions. After validation, the authors characterized these differentially methylated regions using personality trait assessment and functional MRI in a sample of 499 adolescents.

Hypermethylation in the 3-protein-phosphatase-1G (PPM1G) gene locus was associated with alcohol use disorder. The authors found association of PPM1G hypermethylation with early escalation of alcohol use and increased impulsiveness. They also observed association of PPM1G Hypermethylation with increased blood-oxygen-level-dependent response in the right subthalamic nucleus during an impulsiveness task.

Overall, the authors provide first evidence for an epigenetic marker associated with alcohol consumption and its underlying neurobehavioral phenotype.

# Newsflash: Recent publications

## RECENT PUBLICATIONS FROM THE MATRICS CONSORTIUM

**TITLE:** New evidence of factor structure and measurement invariance of the SDQ across five European nations

**AUTHORS:** Ortuño-Sierra, J. et. al

**JOURNAL, YEAR:** European Child & Adolescent Psychiatry, 2015, 24: 1523-1534

The main purpose of the present study was to analyse the internal structure and to test the measurement invariance of the Strengths and Difficulties Questionnaire (SDQ), self-reported version, in five European countries. The sample consisted of 3012 adolescents aged between 12 and 17 years ( $M = 14.20$ ;  $SD = 0.83$ ). The five-factor model (with correlated errors added), and the five-factor model (with correlated errors added) with the reverse-worded items allowed to cross-load on the Prosocial subscale, displayed adequate goodness of-fit indices. Multi-group confirmatory factor analysis showed that the five-factor model (with correlated errors added) had partial strong measurement invariance by countries. A total of 11 of the 25 items were non-invariant across samples. The level of internal consistency of the Total difficulties score was 0.84, ranging between 0.69 and 0.78 for the SDQ subscales. The findings indicate that the SDQ's subscales need to be modified in various ways for screening emotional and behavioural problems in the five European countries that were analysed.

**TITLE:** Rsu1 regulates ethanol consumption in *Drosophila* and humans

**AUTHORS:** Shamsideen A. Ojelade et al.,

**JOURNAL, YEAR:** Proceedings of the National Academy of Sciences, 2015, E4085-E4093

Alcohol abuse is highly prevalent, but little is understood about the molecular causes. Here, we report that Ras suppressor 1 (Rsu1) affects ethanol consumption in flies and humans. *Drosophila* lacking Rsu1 show reduced sensitivity to ethanol-induced sedation. They show that Rsu1 is required in the adult nervous system for normal sensitivity and that it acts downstream of the integrin cell adhesion molecule and upstream of the Ras-related C3 botulinum toxin substrate 1 (Rac1) GTPase to regulate the actin cytoskeleton. In an ethanol preference assay, global loss of Rsu1 causes high naïve preference. In contrast, flies lacking Rsu1 only in the mushroom bodies of the brain show normal naïve preference but then fail to acquire ethanol preference like normal flies. Rsu1 is, thus, required in distinct neurons to modulate naïve and acquired ethanol preference. In humans, they find that polymorphisms in RSU1 are associated with brain activation in the ventral striatum during reward anticipation in adolescents and alcohol consumption in both adolescents and adults. Together, these data suggest a conserved role for integrin/Rsu1/Rac1/actin signaling in modulating reward-related phenotypes, including ethanol consumption, across phyla.



# Newsflash: Recent publications

## RECENT PUBLICATIONS FROM THE MATRICS CONSORTIUM

**TITLE:** The influence of comorbid oppositional defiant disorder on white matter microstructure in attention-deficit/hyperactivity disorder

**AUTHORS:** van Ewijk, H. et al.

**JOURNAL, YEAR:** European Child & Adolescent Psychiatry, 2015, 1-10

Attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) are highly comorbid disorders. ADHD has been associated with altered white matter (WM) microstructure, though the literature is inconsistent, which may be due to differences in the in- or exclusion of participants with comorbid ODD. WM abnormalities in ODD are still poorly understood, and it is unclear whether comorbid ODD in ADHD may have confounded the current ADHD literature. Diffusion Tensor Imaging (DTI) was used to compare fractional anisotropy (FA) and mean diffusivity (MD) between ADHD patients with ( $n = 42$ ) and without ( $n = 117$ ) comorbid ODD. All participants were between 8–25 years and groups did not differ in mean age or gender. Follow-up analyses were conducted to examine the role of antisocial behaviour (conduct problems) on FA and MD values in both groups. Comorbid ODD in ADHD was associated with lower FA in left frontotemporal WM, which appeared independent of ADHD symptoms. FA was negatively associated with antisocial behaviour in ADHD + ODD, but not in ADHD-only. Comorbid ODD is associated with WM abnormalities in individuals with ADHD, which appears to be independent of ADHD symptoms. Altered WM microstructure in comorbid ODD may play a role in inconsistencies in the current DTI literature in ADHD. Altered development of these tracts may contribute to social-emotional and cognitive problems in children with oppositional and antisocial behaviour.

# Newsflash: Aggression in the spotlight

## RECENT PUBLICATIONS ON AGGRESSION RESEARCH

**PUBLICATION:** The neurobiology of aggression and violence.

**AUTHORS:** Rosell, D. R., & Siever, L. J.

**JOURNAL, YEAR:** CNS spectrums, 2015, 20(03): 254-279

Aggression and violence represent a significant public health concern and a clinical challenge for the mental healthcare provider. A great deal has been revealed regarding the neurobiology of violence and aggression, and an integration of this body of knowledge will ultimately serve to advance clinical diagnostics and therapeutic interventions. The authors review the latest findings regarding the neurobiology of aggression and violence. First, they introduce the construct of aggression, with a focus on issues related to its heterogeneity, as well as the importance of refining the aggression phenotype in order to reduce pathophysiologic variability. Next they examine the neuroanatomy of aggression and violence, focusing on regional volumes, functional studies, and interregional connectivity. Significant emphasis lies on the amygdala, as well as amygdala–frontal circuitry. Then attention is turned to the neurochemistry and molecular genetics of aggression and violence, examining the extensive findings on the serotonergic system, as well as the growing literature on the dopaminergic and vasopressinergic systems. The contribution of steroid hormones, namely, cortisol and testosterone, will be addressed. Finally, the findings will be summarized with a focus on reconciling inconsistencies and potential clinical implications; and the authors suggest areas of focus for future directions in the field.

**PUBLICATION:** Current research on conduct disorder in children and adolescents.

**AUTHORS:** Frick, P. J.

**JOURNAL, YEAR:** South African Journal of Psychology, 2016

In this article, research on the various risk factors of conduct disorder is reviewed, with a specific focus on recent theories of how these risk factors can negatively influence a child's development and place him or her at risk for acting in ways that violate the rights of others or that violate major societal norms. Support for several specific developmental pathways, each involving somewhat different risk factors and causal mechanisms, is provided. This research has important implications for how research is conducted and interpreted. It also has important implications for the assessment and diagnosis of conduct disorder. Most importantly, it highlights the need for a comprehensive and individualized approach to treatment that recognizes the different needs of youth across the various pathways.

# Newsflash: Aggression in the spotlight

## RECENT PUBLICATIONS ON AGGRESSION RESEARCH

**PUBLICATION:** Does comorbid anxiety counteract emotion recognition deficits in conduct disorder?

**AUTHORS:** Short, R. M., Sonuga-Barke, E. J., Adams, W. J., & Fairchild, G.

**JOURNAL, YEAR:** Journal of Child Psychology and Psychiatry, 2016

Previous research has reported altered emotion recognition in both conduct disorder (CD) and anxiety disorders (ADs) but these effects appear to be of different kinds. Adolescents with CD often show a generalized pattern of deficits, while those with ADs show hypersensitivity to specific negative emotions. Although these conditions often cooccur, little is known regarding emotion recognition performance in comorbid CD + ADs. Here, the authors test the hypothesis that in the comorbid case, anxiety-related emotion hypersensitivity counteracts the emotion recognition deficits typically observed in CD. They compared facial emotion recognition across four groups of adolescents aged 12-18 years: those with CD alone, ADs alone, cooccurring CD + ADs and typically developing controls. The emotion recognition task we used systematically manipulated the emotional intensity of facial expressions as well as fixation location (eye, nose or mouth region). Conduct disorder was associated with a generalised impairment in emotion recognition; however, this may have been modulated by group differences in IQ. AD was associated with increased sensitivity to low-intensity happiness, disgust and sadness. In general, the comorbid CD + ADs group performed similarly to typically developing controls. Although CD alone was associated with emotion recognition impairments, ADs and comorbid CD + ADs were associated with normal or enhanced emotion recognition performance.

**PUBLICATION:** The clinical usefulness of the new LPE specifier for subtyping adolescents with conduct disorder in the DSM 5

**AUTHORS:** Jambroes, T., Jansen, L. M., Vermeiren, R. R., Doreleijers, T. A., Colins, O. F., & Popma, A.

**JOURNAL, YEAR:** European Child & Adolescent Psychiatry, 2016

In DSM 5, conduct disorder (CD) has been expanded with a new specifier 'with Limited Prosocial Emotions' (LPE) in addition to the age-of-onset (AoO) subtyping, and is thought to identify a severe antisocial subgroup of CD. However, research in clinical practice has been scarce. Thus, the current study will examine differences in clinical symptoms between subtypes of CD, based on both subtyping schemes. Subsequently, it will investigate whether the LPE specifier explains unique variance in aggression, added to the AoO subtyping. CD diagnoses and AoO subtype were assessed in 145 adolescents with CD from a closed treatment institution using a structured diagnostic interview. The LPE specifier was assessed using the callous-unemotional dimension of the Youth Psychopathy Traits Inventory. Self-reported proactive and reactive aggression, rule-breaking behavior and internalizing problems were compared. Youth with childhood-onset CD and LPE showed significantly more aggression than adolescent-onset CD without LPE. Hierarchical regression revealed that the LPE specifier uniquely explained 7 % of the variance in reactive aggression, additionally to the AoO subtyping. For proactive aggression, the interaction between AoO and the LPE added 4.5 % to the explained variance. Although the LPE specifier may help to identify a more aggressive subtype of CD in adolescents, the incremental utility seems to be limited.



# Newsflash: Aggression in the spotlight

## RECENT PUBLICATIONS ON AGGRESSION RESEARCH

**PUBLICATION:** Conduct Disorder/Oppositional Defiant Disorder and Attachment: A Meta-Analysis.

**AUTHORS:** Theule, J., Germain, S. M., Cheung, K., Hurl, K. E., & Markel, C.

**JOURNAL, YEAR:** Journal of Developmental and Life-Course Criminology, 2016, 1-24.

To summarize the literature on and clarify the magnitude of the association between conduct disorder/oppositional defiant disorder (CD/ODD) and attachment and to search for moderators of this relationship.

A meta-analysis was conducted in order to elucidate the potential relationship between attachment style and CD/ODD symptoms and to establish the size of the effect. An extensive literature search was conducted through multiple databases for published and unpublished works.

The main finding from this study indicated that there is a moderate relationship between CD/ODD symptoms and attachment insecurity. The standardized mean difference in attachment insecurity between individuals with and without CD/ODD was large. There was a strong relationship between CD/ODD symptoms and disorganized attachment symptoms. The weighted odds ratio for the presence of disorganized attachment in individuals with and without CD/ODD was large. No significant moderators were identified.

The results of this study demonstrate that individuals with CD/ODD are much more likely to have an insecure or disorganized attachment than individuals without CD/ODD, but that it is not assured.

**PUBLICATION:** Using a Novel Emotional Skills Module to Enhance Empathic Responding for a Child With Conduct Disorder With Limited Prosocial Emotions.

**AUTHORS:** Datyner, A., Kimonis, E. R., Hunt, E., & Armstrong, K.

**JOURNAL, YEAR:** Clinical Case Studies, 2016, 15(1): 35-52.

Children with conduct problems benefit less from empirically supported interventions for disruptive behaviors when callous-unemotional (CU) traits (i.e., lack of empathy/guilt) are also present. Traditional “gold-standard” interventions for disruptive behavior disorders that focus primarily on improving parenting skills fail to address the core deficits in emotional processing and empathic responding unique to children with co-occurring conduct problems and CU traits (CP + CU). This case study presents a follow-up of the treatment of a young boy with severe disruptive behavior and pronounced CU traits using a novel, brief adjunctive treatment called Coaching and Rewarding Emotional Skills (CARES). Findings (a) indicate short-term improvements in empathic responding and emotion recognition with CARES and (b) provide preliminary support for supplementing parent training with a brief adjunctive intervention to improve socio-emotional behavior and CU traits. Novel targeted interventions for children with CP + CU are critically needed given their poor prognosis and long-term impairment.

# Sharing is caring: Upcoming Congresses and Meetings

International Organization of Psychophysiology  
World Congress

**August 31<sup>st</sup> – September 4<sup>th</sup> 2016**

Havanna, Cuba

Abstract deadline: closed

International Association for Child and  
Adolescent Psychiatry and allied Professions  
(IACAPAP) 22<sup>nd</sup> world congress

**September 18<sup>th</sup> -22<sup>nd</sup> 2016**

Calgary, Canada

Abstract deadline: closed

MATRICS Steering Committee Meeting

**October 19<sup>th</sup> -20<sup>th</sup> 2016**

Berlin, Germany

Fifth International Conference on Violence in  
the Health Sector

**October 26<sup>th</sup> -28<sup>th</sup> 2016**

Dublin, Ireland

Abstract deadline: August 1<sup>st</sup> 2016

Society for Neuroscience  
annual meeting

**November 12<sup>th</sup> – 16<sup>th</sup> 2016**

San Diego, USA

Abstract deadline: closed

International Congress of clinical and health  
psychology on children and adolescents

**November 17<sup>th</sup> – 19<sup>th</sup> 2016**

Barcelona, Spain

Abstract deadline: June 16<sup>th</sup> 2016

Organization for Human Brain Mapping  
(OHBM) 2017 Annual Meeting

**June 23<sup>rd</sup> – 29<sup>th</sup> 2017**

Vancouver, Canada

Abstract deadline: January 2017

17<sup>th</sup> International Congress of ESCAP  
(European Society for Child and Adolescent  
Psychiatry)

**July 8<sup>th</sup> – 12<sup>th</sup> 2017**

Geneva, Switzerland

Abstract deadline: December 30<sup>th</sup> 2016

# The MATRICS Consortium:



Kinder- und Jugend-  
psychiatrie / Psychotherapie  
Universitätsklinikum Ulm

