

NEWS

A successful application: neuropattern™ stressdiagnostics shows good results in workplace prevention // Widespread disease depression // Precision medicine – an allocation

Study results regarding
the use of neuropattern™
stressdiagnostics at the
Forestry Department
Rhineland-Palatinate, Germany



Landesforsten
Rheinland-Pfalz

Dear reader,

the positive feedback and encouraging response to the first print edition of the daacro newsletter in summer 2015, leads us to further go on. We will continue to emphasize the high importance of an excellent and competent consultation prior to and during the process of product development. Also, we will continue to inform you about the latest trends and developments in our field of expertise.

In addition, we will introduce you to further members of our team. A good and fruitful collaboration is always about trusting people - next to a high level of expertise and high quality standards!

Further information can be found on our

website. Please contact us at any time!

Looking forward to hearing from you, best wishes

Juliane Hellhammer, PhD
daacro Founder & CEO



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- 6 AUDIOVISUELLE WAHRNEHMUNGS-FÖRDERUNG (SHORT: AVWF)

SAVE THE DATE

FEMNAT-CD

11 - 13 NOVEMBER 2015
BILBAO, SPAIN

FOOD MATTERS LIVE

17 - 19 NOVEMBER 2015
LONDON, UK
BOOTH 146; DAACRO-TALK: NOV 19, 11:25 AM

FOOD INGREDIENTS

01 - 03 DECEMBER 2015
PARIS, FRANCE

PHARMAFORUM

03 MARCH 2016
WIESBADEN, GERMANY

VITAFOODS

10 - 12 MAY 2016
GENEVA, SWITZERLAND
BOOTH N22

46TH ISPNE CONFERENCE

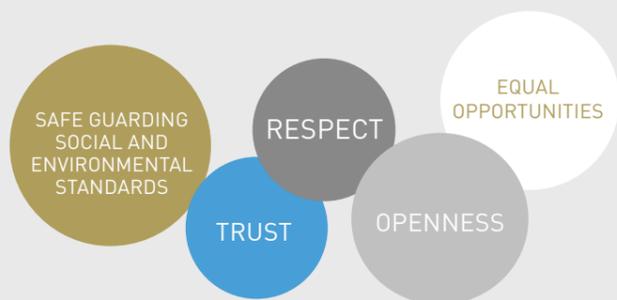
08 - 11 SEPTEMBER 2016
MIAMI, USA

1

DAACRO COMMITS TO THE CODE OF CONDUCT AS SEDEX ADVANCE MEMBER

Many big companies, e.g. Beiersdorf AG, Danone, etc., like to be assured that the service providers and other companies they co-operate with comply with certain social, environmental and ethical standards. These standards are the basis of the code of conduct set by Sedex, a not-for-profit membership organisation dedicated to driving ethical improvements in global supply chains. This code of conduct is the basis of each cooperation. It grounds on a culture of mutual trust and respect, openness, balance of mutual interests and chances. Both parties agree that the preservation of the presented social and environmental standards is the basis for a corporate, lasting and successful future. Compliance with the mandatory behavioural standards is self-evident for daacro – our membership at Sedex* is therefore a logic consequence of our actions. We are happy to meet future demands of our customers and are ready for an audit concept concerning the fulfilment of the code of conduct.

Sedex*: Supplier Ethical Data EXchange



2

STRESS DIAGNOSTICS IN WORKPLACE HEALTH PROMOTION



STUDY RESULTS REGARDING THE USE OF NEUROPATTERN™ STRESSDIAGNOSTICS AT THE FORESTRY DEPARTMENT RHINELAND-PALATINATE, GERMANY

The burden of stress-related health-impairments in the occupational field can result in decreased work productivity, increase in rates of sick leave, cases of early retirement, and higher organizational costs. On an individual level, stress-related symptoms and lower quality of life are reported.

A pilot study suggests that applying neuropattern™ to a non-clinical population and implementing it into early prevention may lead to a significant improvement of psychological health and health related behavior as well as a reduction of perceived stress and emotional exhaustion. Additionally, neuropattern™ was able to sensitively detect functional changes in stress physiology at an early stage suggesting its usefulness within the occupational field for means of early prevention.



3

DEPRESSION – A WIDESPREAD DISEASE! ARE BIOMARKERS IN SIGHT?

AROUND 350 MILLION PEOPLE ALL OVER THE WORLD SUFFER FROM DEPRESSION, WHICH MAKES IT ONE OF THE MOST COMMON MENTAL DISORDERS.

Treatments for depression usually consist of a combination of psychotherapy or counselling and drugs, which can have undesirable side effects. However, more than one-third of patients with depression do not respond properly to treatment with antidepressants, with 20 % of these failing to show any improvement at all whilst on antidepressants (non-responders).

Research is needed, in order to answer the following questions:

Are there alternatives to the currently prescribed drugs, perhaps from the fields of natural medicine or botanical drugs, which cause fewer side effects?

Could combinations of products have better results in non-responders?

Is it possible to define different subgroups of depression and their underlying mechanisms sooner and „tailor“ specific treatments to improve the symptoms more quickly?

While in the past, efficacy studies of antidepressants have been based on information obtained from questionnaires, in recent years there has been a tremendous amount of energy put into research for biomarkers for depression. Benefits for studies are still limited and it seems that THE biomarker for depression doesn't exist. Results from preliminary studies with biomarker panels (several biomarkers that are interpreted together) seem more promising.

It is highly likely that what we generally call

„depression“ today in fact comprises a number of different sub-types of depressive disturbances, each one with its own identifiable biomarkers. It would be logical to assume that different drugs would be needed to treat these different sub-types. This is exactly the goal of precision medicine: previous phenotypical diagnoses are supposed to be replaced by a new taxonomy based on endophenotypes. Endophenotypes combine specific biomarkers with clinically relevant data. One highly promising approach is neuropattern™, a new diagnostic test that is used to differentiate endophenotypes, and suggests the appropriate treatments for individuals. Indeed, conceptual endophenotypes are used currently to differentiate and stratify between various states of exhaustion and depression syndromes.

How can we proceed further? Are biomarker panels like the panel of 9 serum biomarkers (α 1-antitrypsin, apolipoprotein CIII, BDNF (brain-derived neurotrophic factor), cortisol, epidermal growth factor, myeloperoxidase, prolactin, resistin and soluble tumour necrosis factor- α receptor type II) as described by Papakostas et al. (2012) the solution? It will probably take years to state whether particular biomarkers will be useful in clinical practice and benefit a personalized treatment. Until then, it makes sense to work with conceptual endophenotypes (neuropattern™) which facilitate the allocation of such biomarkers to causal neurobiological mechanisms and thus take a leading role in the process of further developing an adequate depression treatment.

Papakostas GI, Shelton RC, Kinrys G, Henry ME, Bakow BR, Lipkin SH, Pi B, Thurmond L, Bilello JA (2013). Assessment of a multi-assay, serum-based biological diagnostic test for major depressive disorder: a pilot and replication study. *Mol Psychiatry*, 18(3):332-9.



4 PRECISION MEDICINE – WHAT IS IT, AND WHAT DOES IT MEAN IN CLINICAL RESEARCH?

EVERY DAY, MILLIONS OF PEOPLE TAKE DRUGS THAT ARE NOT HELPING THEM. THIS IS DUE TO MISSING KNOWLEDGE ON THE SPECIFIC INDIVIDUAL EFFECTS OF CERTAIN SUBSTANCES.

The realization that doctors need to include this individual variability in their considerations leads to an increasing interest in what is known as “precision medicine”. In January 2015, US president Barack Obama announced a „Precision Medicine Initiative“, that would establish a national database of genetic and other health-related data of millions of US citizens. (Schork, 2015)

So what exactly is „precision medicine“? Jameson and Longo (2015) define „precision medicine“ as treatments that are tailored to an individual patient’s particular needs, based on biomarkers, genetic, phenotypical and psycho-social characteristics that differentiate one patient from another with similar symptoms.

What does this personalized approach mean for clinical trials? Clinical trials are routinely based on the assessment of a few parameters from numerous patients. The discovery of a treatment that is effective in a certain subgroup is rare and often an incidental finding. Often, these incidental findings are the result of a disappointing outcome of a large study where researchers investigate why the treatment worked in

some subjects while not in others. This approach is inefficient and costly. One alternative are studies that focus on a single individual, known as N-of-1 studies, in which all kinds of clinical relevant data are obtained from one person. When sufficient data is collected over a long enough period of time and the appropriate control groups are used, it is safe to say whether a particular test person has responded to a treatment or not. The aggregated results of many N-of-1 studies that were all carried out under the same conditions provide information that may lead to better treatment for subgroups of the population, if not the entire population. (Schork, 2015)

Conclusion: Well-designed, sophisticated N-of-1 trials should contribute to classical clinical trials confirming the efficacy of tailored treatment. In line, adequate biomarkers, monitoring devices, study designs and data analyses need to be developed.

Jameson JL, Longo DL (2015). Precision medicine-*personalized, problematic, and promising*. *N Engl J Med*, 372(23):2229-34.

Schork NJ (2015). *Personalized medicine: Time for one-person trials*. *Nature*, 520(7549):609-11.

STRESS AND COGNITION



5 CLINICAL TRIALS AND COGNITIVE TESTING

DIFFERENT AREAS OF APPLICATION REQUIRE SPECIFIC TEST PROFILES

COMPUTERIZED TESTS HAVE BECOME THE GOLD STANDARD WHEN IT COMES TO MEASURING COGNITIVE FUNCTION. NEVERTHELESS, THE FIELD OF APPLICATION MIGHT DIFFER DEPENDING ON WHETHER YOU ARE TESTING IN A RESEARCH, CLINICAL TRIAL, OR HEALTHCARE SETTING.

Cognitive research needs highly sensitive tools that have been proven to measure brain function across cognitive domains and specific neural systems. Clinical trials may wish to target the key cognitive domains that are commonly affected by pharmacological manipulation, allowing assessment of efficacy as well as safety aspects of an investigational compound. Healthcare focuses on optimizing mental wellbeing and performance throughout life. By sensitively measuring cognitive performance, people with mental health disorders can be identified earlier, access treatments faster, and stay healthy for longer, improving quality of life and reducing costs.

WITH US FROM THE BEGINNING

Our employees continuously upgrade their qualifications:



Nadin Meyer,
Quality Manager

Nadin holds a Diploma (MSc) of the University of Trier. Her special area of expertise is in the field of cognitive function. For daacro she has worked for many years as Senior Study Manager, now acting as quality manager.



Christof Zintel,
Software Developer

Christof is an expert in electronic data processing. He develops neuropattern™-software and programs software solutions for daacro’s clinical trials allowing real time assessment in our studies. His activities are closely linked to daacro’s data management.

EU PROJECT FEMNAT-CD

SALIVA LAB TRIER DELIVERS FIRST RESULTS WITHIN THE EU-CONSORTIUM FEMNAT-CD

daacro has just finished analyzing the first batch of saliva samples for the FP7-funded research project: "Neurobiology and Treatment of Adolescent Female Conduct Disorder: The Central Role of Emotion Processing" (FemNAT-CD) with 17 European partners including 13 Universities and 4 small and medium enterprises. In total 636 baseline saliva samples were analysed for cortisol, alpha-amylase, testosterone, estradiol, progesterone and DHEA-S. In addition samples from 132 sets of samples from the Trier Social Stress Test (TSST) were analysed for cortisol and testosterone. First results of the TSST were presented in September 2015 at the annual meeting of ISPNE (International Society for Psychoneuroendocrinology) in Edinburgh, UK. Further results will be presented at the 3rd FemNAT-CD General Annual Meeting in Bilbao, Spain, in November 2015.



FRESH OFF THE PRESS

First TSST-results of the EU-funded FemNAT-CD study: Neuroendocrinological stress response to acute psychosocial stress in children and adolescents with conduct disorder compared to healthy controls. Bernhard, A., Martinelli, A., Ackermann, K., Kirschbaum, C., Hellhammer, J., & Freitag, C.M.

Poster presentation at the 45th Annual Meeting of the International Society of Psychoneuroendocrinology, Sept 08-10, 2015, Edinburgh, UK.

In a cooperation between the Behavioral and Molecular Neurobiology Department of the University Regensburg and the contract research organization daacro in the Science Park Trier, oxytocin- und stress expertise was combined. The result was published in the scientific journal Psychoneuroendocrinology:

Salivary oxytocin concentrations in response to running, sexualself-stimulation, breastfeeding and the TSST: The Regensburg Oxytocin Challenge (ROC) study. Trynke R. de Jong, Rohit Menon, Anna Bludau, Thomas Grund, Verena Biermeier, Stefanie M. Klampfl, Benjamin Jurek, Oliver J. Bosch, Juliane Hellhammer & Inga D. Neumann. Psychoneuroendocrinology 62 (2015) 381-388.

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6 ANALYSIS OF EXTERNAL DATA OBTAINED FROM STRESS MEDICINE:

FIRST RESULTS ON THE USE OF AVWF-NEUROCOACHING® IN PATIENTS

In addition to our main activity – the conduct of clinical studies – we provide subservices of clinical studies, such as the statistical analysis of external data. Thus, the „Audio Visuelle Wahrnehmungsförderung“ (AVWF), a method developed by Ulrich Conrady and successfully used in sportsmen to improve their physical performance was applied in a patient population to analyze its effects. AVWF is thought to positively influence and balance the autonomous nervous system via sound waves. It is thought that AVWF can impact on overstimulation and disease-causing stress in work and everyday life.

In an explorative analysis, the cortisol awakening response (CAR) of 44 patients of the clinic Lipperland (rehabilitation center of the German pension insurance, medical director Dr. Dieter Olbrich) was assessed. Half of the patients passed through the usual clinical activities, whereas the other half was additionally treated with AVWF. The biologically active fraction of cortisol was measured in saliva. Normally, a typical 70 % rise in cortisol levels can be observed after waking up in healthy subjects. This can be altered by stress (see figure 1).

Three examples for a cortisol awakening response (CAR)

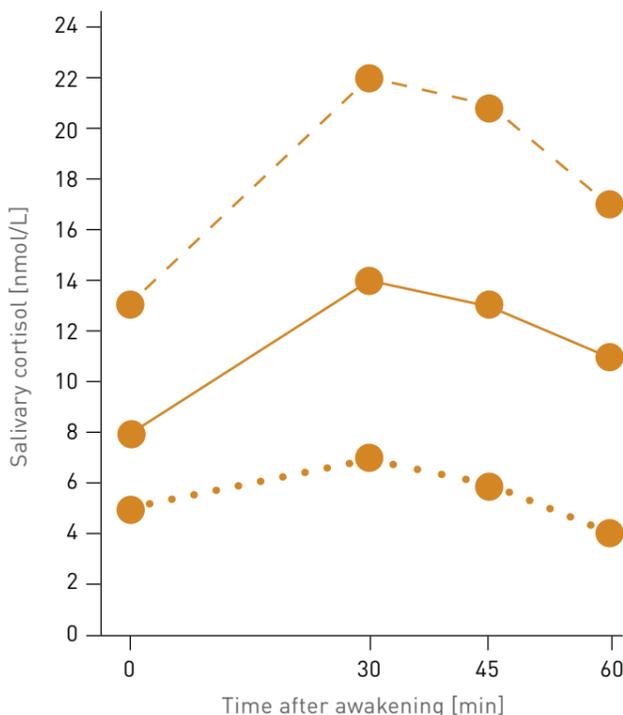


Figure 1: The graphic represents a typically seen „normal“ CAR, a blunted CAR (dotted line, hypocortisolism) and a hyperresponsive CAR (dashed line, hypercortisolism).

COMING SOON:

Shortly, the following publication will appear in Elsevier's Journal of Psychoneuroendocrinology: Assessment of the cortisol awakening response: an expert consensus report.

This publication describes the current standard on how to achieve reliable data on the cortisol awakening response and serves as a guide for every scientist planning a study that includes the CAR as an endpoint.

Data analysis of these patients revealed a trend towards a reduction of the CAR in AVWF treated patients as compared to those receiving the regular treatment of the clinic. Furthermore, patients with a blunted CAR showed a raise of their CAR after AVWF intervention, whereas patients with a hyperresponsive CAR showed a decline of their CAR in response to AVWF treatment. Taken together, these first observational findings suggest that adding an AVWF intervention to the regular rehabilitation program can further add value for the patients by normalizing their CAR.

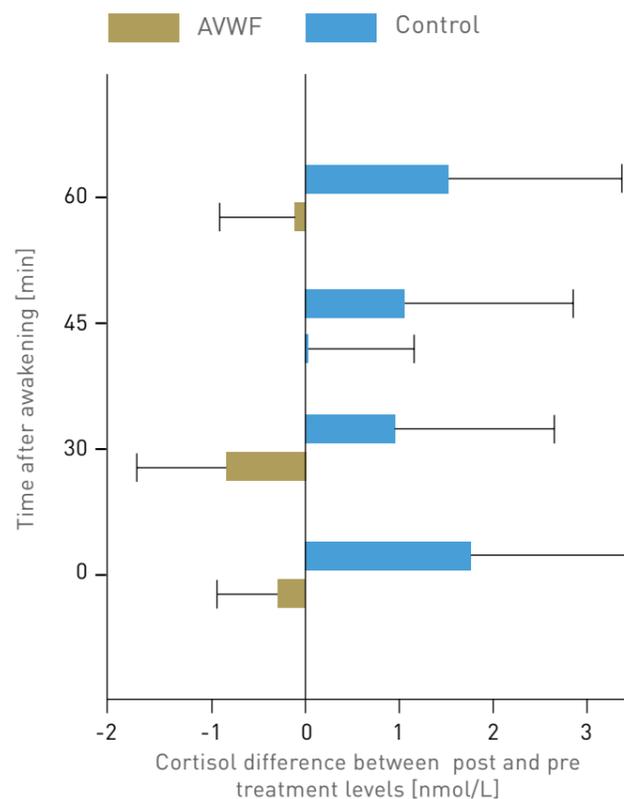


Figure 2: The graphic represents the delta of the CAR between clinic admission and discharge at four time points after awakening and for AVWF treated patients as well as their controls.

TRIER – LAS VEGAS

Juliane Hellhammer presented study results on stress dampening effects of Lipogen PSPA™ (phosphatidylserine + phosphatidic acid) consumption on the Supply Side West in Las Vegas. The exhibition ranks among the biggest meetings of food supplement producers worldwide. In October 2015 over 1,200 exhibitors and 14,000 visitors from 66 countries attended the exhibition.



From left to right: Ariel Gordon, Dr. Juliane Hellhammer, Ilan Perry, David Rutenberg.



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