Personalized nutrition in clinical studies: methodological approaches

Juliane Hellhammer, PhD

daacro – Full Service CRO – booth 690
Precision Medicine Initiative launched by President Barack Obama in 2015

„ ... to give us all access to the personalized information we need to keep ourselves and our families healthier.“
State of the Union Address 2015; 20. Januar 2015

We define precision medicine as treatments targeted to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentation. Inherent in this definition is the goal of improving clinical outcomes for individual patients.“ (Jameson & Longo, NEJM, 2015: 372;23, 229)

This might refer to nutrients and healthy subjects, as well. Especially since the demarcation line between food and drug can be blurry.
“Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease“

National Research Council of the National Academies of Sciences, 2011
Personalized nutrition - but how?

(1) Diagnostics at a point-of-need?
✓ Assessment of individual’s nutritional status and micronutrient

(2) Big data and digital phenotypes?
✓ So far, little evidence that this can provide predictive dietary recommendations for individuals

(3) N=1 trials?

(4) Conceptualization of relevant mechanisms

An example: (2) Big data

Zeevi et al., 2015, Cell 163, 1079-1094
(3) Scientific and clinical benefit of N=1 trials

Time for one-person trials

Precision medicine requires a different type of clinical trial that focuses on individual, not average, responses to therapy, says Nicholas J. Schork.
Gut-brain crosstalk

- Interaction plays an important role in gastrointestinal function and microbiota are important for a normal healthy brain function.
- Alterations of this complex, bidirectional communication system influence homeostasis and promote the risk of disease development.
- This includes not only pathophysiology but multiple effects on overall behavior as affect, motivation, higher cognitive functions …
Mental stress and mood disorders are on the rise due to increasing pressure exerted by modern lifestyle.

Stress-induced behavioral and physiological changes modulate brain activity and promotes many diseases.

High co-morbidity between stress-related symptoms and gastrointestinal, cardiovascular, metabolic or inflammatory disorders.
„Knowledge Networks“ should use conceptual endophenotypes
(4) targeting stress endophenotypes

neuropattern™ conceptualizes endophenotypes of the stress response network by:

- merging available knowledge of dysregulations of noradrenergic, serotonergic, autonomic, HPA-axis systems;
- being conceptualized as specific patterns of psychological, biological and symptomatic measures;
- considering the exposome (pre-/post natal stress and the history of stressors);
- continuously being updated from „knowledge networks“ (e.g. genetic and epigenetic measures), at the same time stimulating biomedical research;
- generating individualized treatment recommendations.
Stratified nutrition in line with allocation to one of the 13 neuropatterns

<table>
<thead>
<tr>
<th>Axes</th>
<th>Systems</th>
<th>Function</th>
<th>Nutrients</th>
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</thead>
<tbody>
<tr>
<td>Glandotropy</td>
<td>CRF, ACTH, Cortisol</td>
<td>energy supply of the brain</td>
<td>Example: phospolipids</td>
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<tr>
<td>Ergotropy</td>
<td>norepinephrine, epinephrine</td>
<td>enhancement of cognitive and physical performance</td>
<td>Example: tyrosine</td>
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<tr>
<td>Trophotropy</td>
<td>serotonin, vagus</td>
<td>regeneration, resilience, relaxation</td>
<td>Example: tryptophan</td>
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W.R. Hess
Swiss Nobel Laureat

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Juliane Hellhammer
The neuropattern™ testset

- Questionnaires include medical history, pre-/postnatal stress, etc.
- Saliva assessment (two diurnal cortisol profiles plus low-dose dexamethasone test on the third day)
- Heart rate variability (evening vs morning assessment)
The neuropattern™ analysis of dysregulation

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<th>pattern</th>
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<td>criteria for neuropattern™ fulfilled</td>
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- Ergotropic sys
- Glandotropic sys
- Trophotropic sys
The ActiveNutraLife Project
(funded by Eurostars Programm no. 01QE1654)

- Joint project of two French and one German company: Bionov producing a unique melon extract with antioxidant effects, V@si developing tailored sports programs and daacro providing neuropattern™
- Aim of the project: a novel medical approach fighting cancer related fatigue after chemotherapy by combining a diagnostic system, a nutritional supplement (NL) and an activity program
- neuropattern™ discriminates 6 different types of fatigue by conceptual endophenotypes of NA-hypoactivity, CRF-hypoactivity, cortisol hypoactivity, CRF hyperactivity, cortisol receptor resistance, serotonin hyperreactivity.
Next steps of the *ActiveNutraLife* Project

- Adapting and expanding neuropattern™ to inflammation biomarkers
- Sept 2017: in a clinical trial neuropattern™ will characterize subtypes of cancer related fatigue and promote a personalized approach (pre-treatment analysis)
- neuropattern™ will quantify treatment success (post-treatment analysis)
- Results in 2018/2019
- Not quite personalized but a clustered dietary advise approach.
„Knowing is not enough; we must apply. Willing is not enough; we must do!“

Goethe (Maxim of the National Academy of Sciences, USA)

Chambers et al., JAMA, 2016

Key Areas of Synergy
- Evolution of evidence base for precision medicine and implementation science
- Recognition of underuse and overuse of interventions
- Management of abundance of data

Optimal integration of effective diagnosis, prevention, and treatment
- Understanding of multilevel context
- Theories and strategies to drive health care improvement

Key Areas of Synergy
- Support for implementation of effective practices
- Contextually sensitive improvement of practices

Optimal use of genomics and behavioral data to drive clinical and patient decision making
- Ongoing development of genomics evidence base
- Personalized and population impact

Key Areas of Synergy
- Refresh cycle of evidence base
- Determination of degree of achievable personalization of care

Use of ongoing data to drive health system improvement
- Focus on iterative and ongoing learning
- All stakeholders participate

Improved health, health care, and health systems
daacro Network

Bringing the best together

Network partners

- daacro Scientific Advisory Board
- Institute of Stress Medicine Trier
- Hospitals
- Medical Laboratories
- Partners for Phase I Studies
- International Universities
- Partners of the Horizon 2020 Programme
- Partners of the FP7 Programme
  - both funded by the European Commission
Thank you for your attention!

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