European Network on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (*EUROMENE*)

COST action CA15111

Deliverable 13

Protocol and guidelines for ME/CFS subgroups detection (stratification) according to the presence of symptoms and subject to potential biomarkers variation

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ME/CFS subgroup detection/stratification according to symptoms and biomarkers

ME/CFS subgroups - What is known?

In the joint session of WG 2 and WG4 at the EUROMENE meeting in Berlin on 19.11.19 the topic was subgroups in ME/CFS. Clinical evidence for existence of subgroups was discussed. Pawel Zalewski from Poland gave an overview on testing of autonomous nervous system dysfunction and results in ME/CFS. WG2 reviewed and discussed recent biomarker studies.

The results are published:

- Clinical subgroups (Expert consensus paper)
- Autonomic assessment (Slomko et al. J Clin Med 2020)
- Biomarker (Recommendations for a public health European wide approach)

ME/CFS subgroup detection/stratification according to biomarkers: cytokines

Medium	Biomarker	Clinical Subgroup	Source
Blood (B)	Prominent activation of pro- and anti-inflammatory cytokines and dissociation of intercytokine regulatory networks (most impotantly ↑ IFNγ as well as ↓ and dissociation from normal intercytokine regulation of CD40)	≤ 3 years duration of illness vs. ≥3 years duration of illness vs. healthy controls	Hornig et al. 2015
B	↑ IL-7 and ↑ IL-8 and↑ IFN-γ	Housebound/Severe cases vs. mobile/moderate cases vs. healthy controls	Hardcastle et al. 2015
B	↓ IL-6 and ↑ RANTES	Mobile/Moderate cases vs. housebound/severe cases vs. healthy controls	Hardcastle et al. 2015
B	↑ IL-10	Female patients with CFS with more somatic symptoms as measured by SCL-90-R vs. female healthy controls vs. female CFS patients with less somatic symptoms	Groven et al. 2018

ME/CFS subgroup detection/stratification according to biomarkers: gene variants/expression/epigenes

B	Existence of autoimmunity-risk SNPs in CTLA4 and PTPN22	Infection-triggered onset vs. non-infectious onset vs. healthy controls	Scheibenbogen et al. 2020
B	↓ α-2A mRNA for at least 48 h after moderate exercise	CFS patients, most of them with orthostatic intolerance vs. healthy controls vs. CFS patients most of them without orthostatic intolerance	Light et al. 2012
B	Different methylation patterns of immune response genes	4 different subtypes were distinguished from each other in regard of differences in physical functioning and post exertional malaise	De Vega et al. 2018

ME/CFS subgroup detection/stratification according to biomarkers: metabolomics

B	**Changes in these metabolic pathways: Fatty Acid Oxidation, Vitamin C/Collagen, Bile acids, Endocannabinoids, Vitamin B12, Amino sugars**	**Females with CFS vs. males with CFS vs. healthy controls)**	**Naviaux *et al.* 2016**
B	Changes in these metabolic pathways: Serine/1-Carbon Metabolism, SAM/SAH/Met, Very Long Chain Fatty Acid Oxidation, Propiogenic Amino Acids, Threonine	Males with CFS vs females with CFS vs. healthy controls)	Naviaux *et al.* 2016
B	↑ Ceramides, ↑ Phosphatidylethanolmines,	With IBS-comorbidity vs. without IBS-comorbidity vs. healthy controls	Nagy-Szakal *et al.* 2018

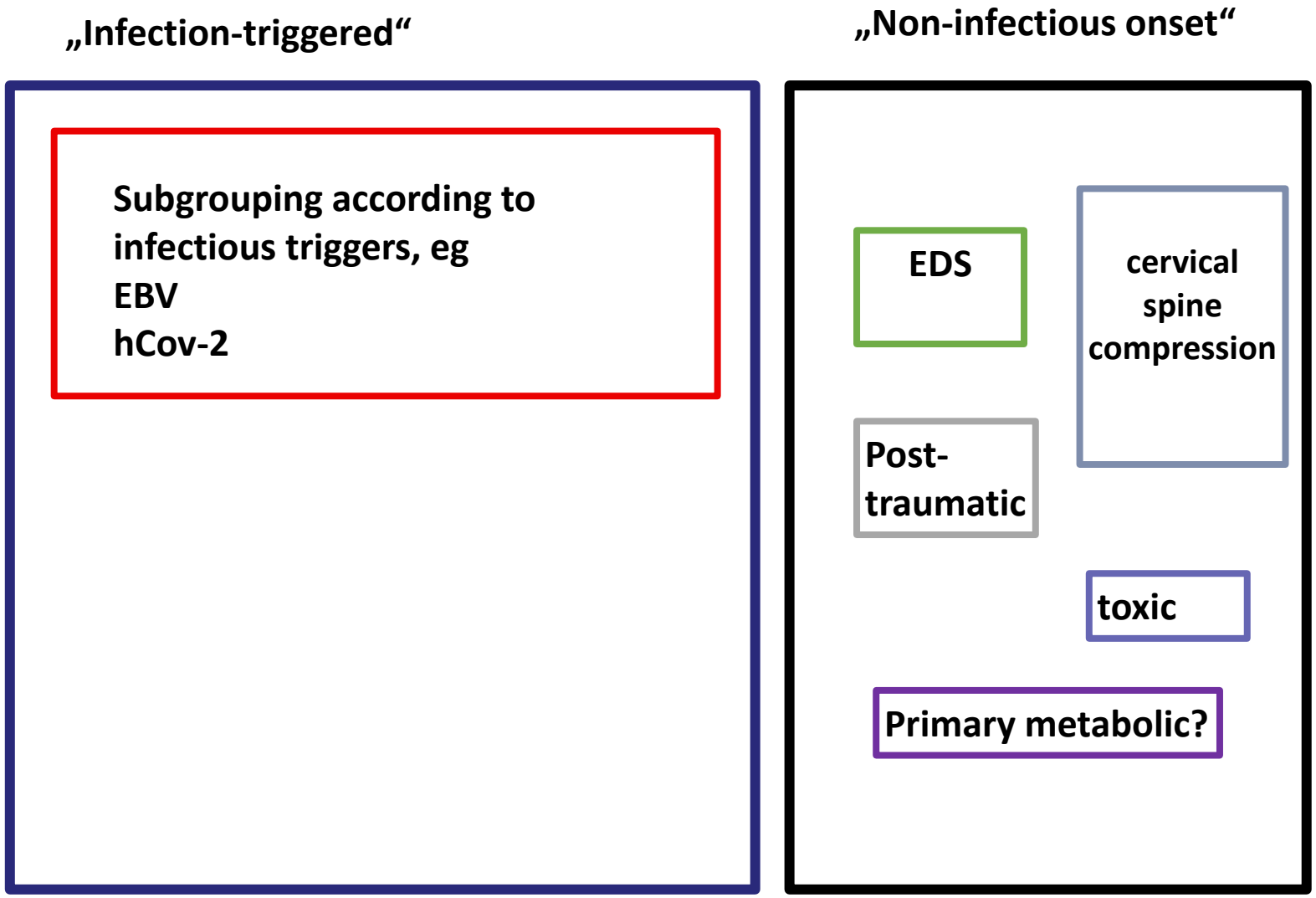
ME/CFS subgroup detection/stratification according to biomarkers: microbiome

Faeces (F)	↑ Abundance of unclassified Alistipes and decreased Faecalibacterium	With IBS-comorbidity vs. without IBS-comorbidity vs. healthy controls	Nagy-Szakal et al. 2017
F	↓ Relative abundance of Bacteroides vulgatus	Without IBS-comorbidity vs. with IBS-comorbidity vs. healthy controls	Nagy-Szakal et al. 2017

Summary studies on ME/CFS - Subgroups

sex	Male - female	Metabolomics	Naviaux, 2016
onset	Infectious vs non-infectious	Autoimmune SNPs	Steiner S, 2020
Disease duration	➢ 3 – 4 years ➢ > 4 years	Cytokines Heart rate/POTS	Hornig Lee Jihyun, 2020
Disease severity	➢ Mild/moderate ➢ severe	Cytokines	Hardcastle, 2015
comorbidity	IBS	microbiome	Nagy-Szakal, 2018

ME/CFS: suggested further subgrouping according to onset




Any questions?


Existing ME/CFS biobanks
in Europe via web


ME/CFS epidemiology survey
from EUROMENE countries
Survey data received
Survey data not received