Trimethylamine N-oxide (TMAO) as a Potential Biomarker of Individual Severe Stress Perception in Posttraumatic Stress Disorder (PTSD)-vulnerable Patients after Acute Myocardial Infarction

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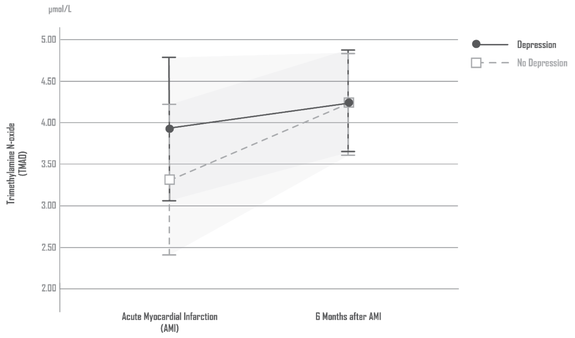
Background, objective and methods

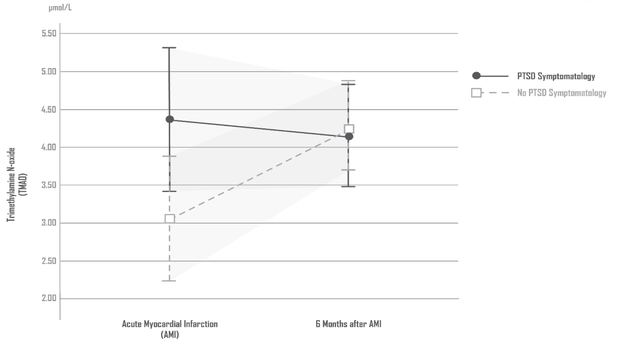
Background: Acute myocardial infarction is not only a somatic disease but potentially triggers psychological effects, too. PTSD is a common stress-related disorder characterized by numerous symptoms, such as flashbacks, intrusions, nightmares and severe anxiety, as well as uncontrollable thoughts and feelings related to the traumatic experience. However, with regard to the development of PTSD, individual stress perception might be crucial since not every serious traumatic experience leads to PTSD. To date, almost no biological correlates of an individual's perception of stress have been identified as being associated with the long-term development of PTSD.

Objective: To determine whether blood levels of TMAO vary immediately after AMI. Furthermore, we investigated whether TMAO is a potential biomarker that might be useful long term predictor of PTSD symptomatology in **Methods:** 114 AMI patients were assessed with standardized clinical psychiatric interviews based on the Hamilton Depression Scale (HAMD-17) after admission to the hospital and 6 months later. In addition, the CAPS-5 was used to explore PTSD symptoms 6 months after AMI. To assess patients' TMAO status, serum samples were collected at hospitalization and 6 months after AMI.

Levels of TMAO in patients with and without depression



Levels of TMAO in pat with and without PTSD symptomatology



Trial design

Category		Total Sample (n=114)	p	PTSD-Symptomatology (n=49/114, 43%)	No PTSD (n=65/114, 57%)	p
Sex						
Male	n (%)	96 (84.2%)	$\chi^2 = 53.368$, df = 1 p < .001[a]	39 (79.6%)	57 (87.7%)	$\chi^2 = 1.38$, df = 1 p = 0.24[a]
Female	n (%)	18 (15.8%)		10 (20.4%)	8 (12.3)	
Age	mean (SD)	59.99 (±11.48)	-	59.2 (±11.52)	60.6 (±11.51)	t = 0.650, df = 112 p = 0.52[b]
Marital Status						
Single	n (%)	14 (12.3%)	$\chi^2 = 117.643$, df = 3 p < .001[a]	8 (17%)	6 (78.5%)	$\chi^2 = 7.17$, df = 3 p = 0.07[a]
Married	n (%)	77 (67.5%)		26 (55.3%)	51 (9.2%)	
Widowed	n (%)	4 (3.5%)		2 (4.3%)	2 (3.1%)	
Divorced	n (%)	17 (14.9%)		11 (23.4%)	6 (9.2%)	
Employment Status						
Paid Work (full- or part-time)	n (%)	53 (46.5%)	$\chi^2 = 87.754$, df = 3 p < .001[a]	21 (42.9%)	32 (49.2%)	$\chi^2 = 7.85$, df = 3 p = 0.05[a]
Homemaker	n (%)	3 (2.6%)		0 (0%)	3 (4.6%)	
Retired	n (%)	54 (47.4%)		24 (49%)	30 (46.2%)	
Unemployed	n (%)	4 (3.5%)		4 (8.1%)	0 (0%)5	
Previous Mental Illness other than PTSD (Depression, Adjustment Disorders, Burn-out)	n (%)	14 (12.3%)	-	8 (16.3%)	6 (9.2%)	$\chi^2 = 1.306$, df = 1 p = 0.25[a]
Previous Psychopharmacological Medication	n (%)	11 (9.6%)	-	5 (10.2%)	6 (9.2%)	$\chi^2 = 0.03$, df = 1 p = 0.86[a]
Substance Abuse						
Alcohol	n (%)	1 (0.87%)	-	1 (2.0%)	0 (0%)	$\chi^2 = 2.09$, df = 1 p = 0.35[a]
Illicit Drugs	n (%)	0 (0%)	-	0 (0%)	0 (0%)	-

Anthropometry, MI characteristics and risk factors

Category		Total Sample (n=114)	p	PTSD-Symptomatology (n=49/114; 43%)	No PTSD (n=65/114; 57%)	
Anthropometry						
Height (cm)	Mean (SD)	174.94 (±8.252)	-	173.5 (±8.27)	176.0 (±8.14)	t = 1.579, df = 110 p = 0.12[a]
Weight (kg)	Mean (SD)	87.01 (±14.38)	-	87.7 (±16.82)	86.5 (±12.32)	t = -.446, df = 109 p = 0.66[a]
BMI	Mean (SD)	28.31 (±-4.0)	-	29.01 (±4.89)	27.76 (±3.07)	t = -1.643, df = 108 p = 0.103[a]
Renal Function						
Glomerular Filtration Rate	Mean (SD)	84.69 (±17.87)	-	83.6 (±18.89)	85.53 (±17.17)	t = 0.578, df = 112 p = 0.56[a]
Cardiac Situation at the Time of Admission to the Hospital						
NSTEMI	n (%)	43 (37.7%)	-	20 (40.8%)	23 (35.4%)	$\chi^2 = 0.351$, df = 1 p = 0.55[b]
STEMI	n (%)	71 (62.3%)		29 (59.2%)	42 (64.6%)	
AMI-related Reanimation	n (%)	3 (2.6%)	-	2 (4.1%)	1 (1.5%)	p = 0.576[c]
PCI-related Parameters						
TIMI Flow before PCI:						
0-I	n (%)	85 (74.6%)	p < .001[a]	35 (76.1%)	50 (84.7%)	$\chi^2 = 1.325$, df = 2 p = 0.52[b]
II	n (%)	15 (13.2%)		8 (17.4%)	7 (11.9%)	
III	n (%)	5 (4.4%)		3 (6.5%)	2 (3.4%	
TIMI flow after PCI:						
0-I	n (%)	4 (3.5%)	p < .001[a]	0 (0%)	4 (6.3%)	$\chi^2 = 4.269$, df = 2 p = 0.12[b]
II	n (%)	8 (7%)		5 (10.6%)	3 (4.7%)	
III	n (%)	99 (86.8%)		42 (89.4%)	57 (89.0%)	
Multivessel PCI	n (%)	23 (20.2%)	-	13 (27.7%)	10 (16.7%)	$\chi^2 = 1.887$, df = 1 p = 0.17[b]
In-hospital Outcome						
Major Bleeding	n (%)	0 (0%)	-	0 (0%)	0 (0%)	-
Reinfarction	n (%)	2 (1.8%)	-	1 (2.0%)	1 (1.5%)	$\chi^2 = 0.042$, df = 1 p = 0.84[b]
Left-Ventricular Ejection Fraction (%)	Mean (SD)	53.15 (±10.559)	-	53.24 (±11.73)	53.07 (±9.60)	t-test = -0.074, df = 79 p = 0.94[a]
Cardiac Risk Factors						
Known CAD	n (%)	18 (15.8%)	-	9 (18.8%)	9 (13.9%)	p = 0.55[b]
Nicotine Abuse	n (%)	39 (34.2%)	-	23 (46.9%)	30 (46.2%)	p = 0.93[b]
Peripheral Arterial Disease	n (%)	3 (2.6%)	-	2 (4.1%)	1 (1.5%)	p = 0.41[b]
IDDM	n (%)	2 (1.8%)	-	1 (2.0%)	1 (1.5%)	p = 0.84[b]
NIDDM	n (%)	17 (14.9%)	-	11 (22.4%)	6 (9.2%)	p = 0.05[b]
Hypertension	n (%)	102 (89.5%)	-	42 (85.7%)	60 (92.3%)	p = 0.26[b]
Hyperlipidemia	n (%)	59 (51.8%)	-	28 (56.0%)	31 (47.7)	p = 0.30[b]
Positive Family History	n (%)	23 (20.2%)	-	10 (23.3%)	13 (25.5%)	p = 0.80[b]
Previous MI	n (%)	12 (10.5%)	-	8 (16.3%)	4 (6.5%)	p = 0.096

Legend: [a] t-test; [b] χ^2 - test, [c] Fisher exact; AMI = Acute Myocardial Infarction; IDDM = Insulin-dependent Diabetes Mellitus; NIDDM = Non-Insulin-dependent Diabetes Mellitus

Conclusions

An elevated TMAO level immediately after AMI might reflect severe stress in PTSD-vulnerable patients, which might also lead to a short-term increased gut permeability to trimethylamine (TMA), the precursor of TMAO. Thus, elevated TMAO might be a biological correlate for stress that is associated with vulnerability to PTSD and might help to identify patients at increased risk.