

PUSAT STUDI BIOETIK DAN
HUKUM KEDOKTERAN ISLAM

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Materi Seminar & Workshop

ISLAMIC SPIRITUAL MEDICINE :
JAMAN NABI DAN JAMAN NOW



Biomarkers for Spirituality?

Genetics and Epigenetics perspectives

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- Spirituality and Religiousness
- Spirituality and Health; Neurophysiology of Spirituality
- Biomarkers for Spirituality; Genetics, Epigenetics, PsychoNeuroImmunological (PNI) markers
- Spiritual CAM Interventions and changes in gene expression
- Research gaps; Proposing the question

Spirituality and Religiousness?

Spirituality: consisting of or having the nature of spirit; intangible/immaterial

Spirituality involves as its central tenet a connection to something greater than oneself

An agnostic can be spiritual



Religion: constitutionalization of spiritualism, an organized belief system promulgated and sustained by a human institution, ethnic group, tribe or culture and involves definite rules of behaviour, practices and rituals.



Spirituality and physical health

- Cardiovascular:

- religiously committed nuns in Italy maintained stable diastolic blood pressure during 30 years' observation (Timio et al., 1997).
- older adults attending religious services more frequently had better functional recovery from acute myocardial infarction (Martin, 2006).
- non-attendees of religious services more likely to have elevated white blood cell counts, highly elevated C-reactive protein, and elevated fibrinogen (King et al., 2001).

- Endocrine:

- routine periodic religious fasting in of Mormons of Utah ($n = 448$) associated with lower diabetes prevalence (Horne et al., 2008).

Spirituality and mental health

Depression. Meta-analysis (98,975 subjects) (Moreira-Almeida, et al., 2006). Religiousness is modestly but robustly associated with lower level of depressive symptoms.

- Extrinsic religious orientation and negative religious coping had a positive association with high frequency of depressive symptoms.
- Intrinsic religious orientation was associated with low levels of depression.

Schizophrenia, suicide, drug abuse (Mohr, et al., 2006):

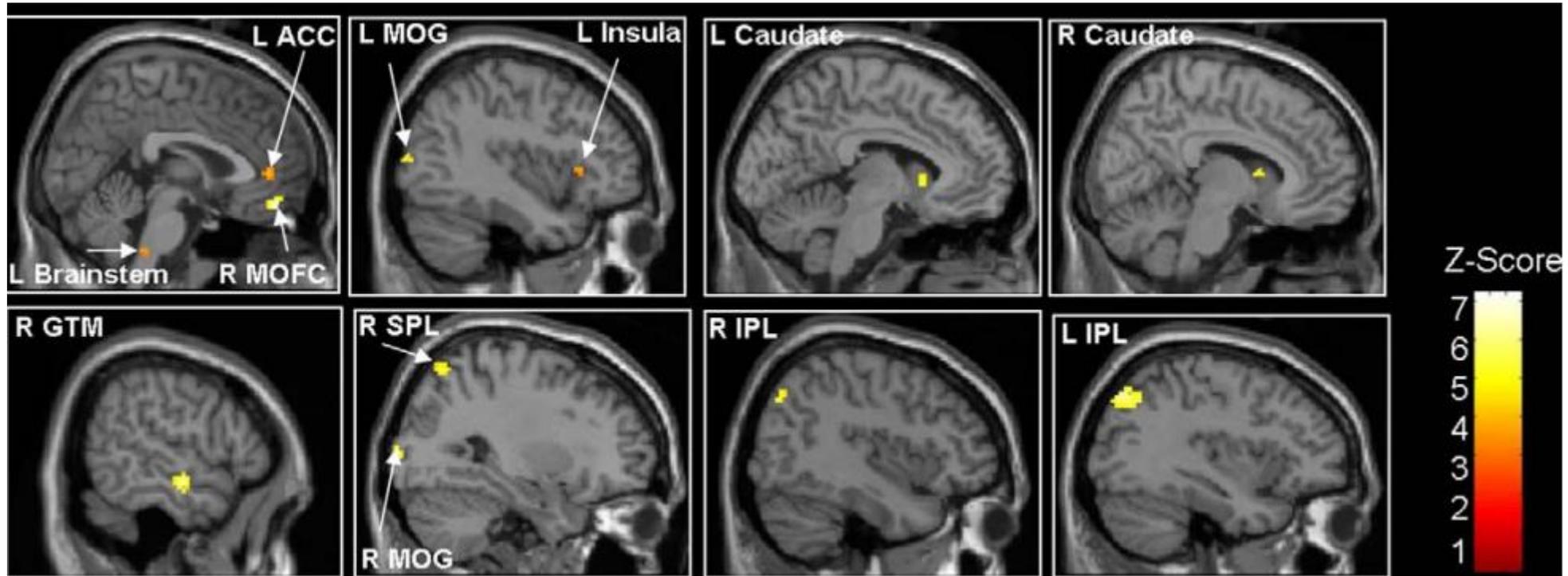
- Religion was used as a positive way of coping by 71% of patients and as a negative way of coping by 14%.
- Religion and spirituality lessened (54%) or increased (10%), psychotic symptoms.
- Religiousness may reduce (33%) or increase (10%), the risk of suicide attempts.
- Religiousness may also reduce (14%) or increase (3%), substance use and foster adherence to (16%) or be in opposition to (15%), psychiatric treatment

Spirituality and mental health

- Subjects (n = 1,046) with high spirituality and high religiousness had better psychological, social relationship and environment, optimism and happiness outcomes as compared to those with low spirituality/low religiousness and those with high spirituality/low religiousness (Vitorino et al., 2018).
- Happiness was positively predicted by generation of personal meaning and transcendental awareness (Amirian, 2016)

Neurophysiology of Spirituality

- Is there God's Spot in the brain? (Beauregard and Paquette, 2006)



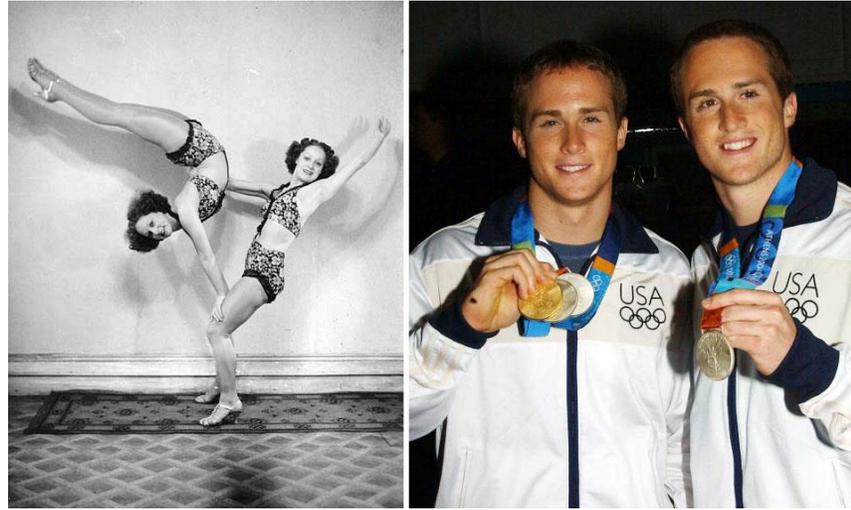
fMRI scans of Carmelite nuns during “union with God” (religious/spiritual/mystical experiences). Significant loci of activation in the right medial orbitofrontal cortex, right middle temporal cortex, right inferior and superior parietal lobules, right caudate, left medial prefrontal cortex, left anterior cingulate cortex, left inferior parietal lobule, left insula, left caudate, and left brainstem.

Neurophysiology of spirituality

Neurochemical	Observed change
Dopamine	Increased
Serotonin	Increased
Melatonin	Increased
DMT	Increased
Noradrenaline	Decreased
Acetylcholine	Increased
Glutamate	Increased
NAAG	Increased
GABA	Increased
Cortisol and CRH	Decreased
AVP	Increased
β -endorphin	Increased

- What neurochemistry/neurotransmitters?
(Mohandas, 2008)

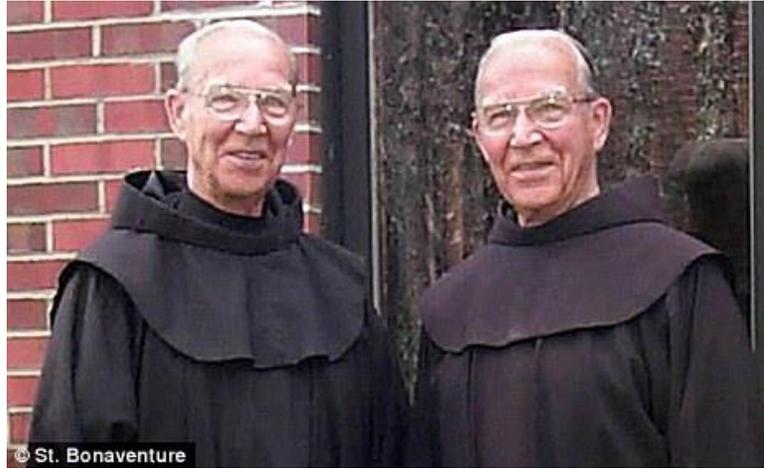
Twin Study - Intelligence



Intelligence (212 subjects):

(Devlin et al., 1997) Nat	Identical Twins	Siblings
Raised Together	85%	45%
Raised Apart	74%	24%

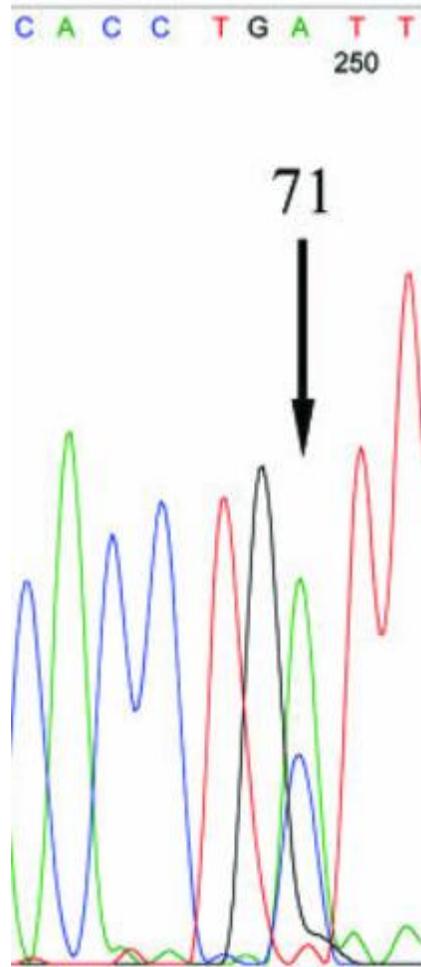
Twin Study - Religiousness



Koenig et al., 2005	Monozygotic Twins	Dizygotic Twins
Retrospective	69%	59%
Current	62%	42%

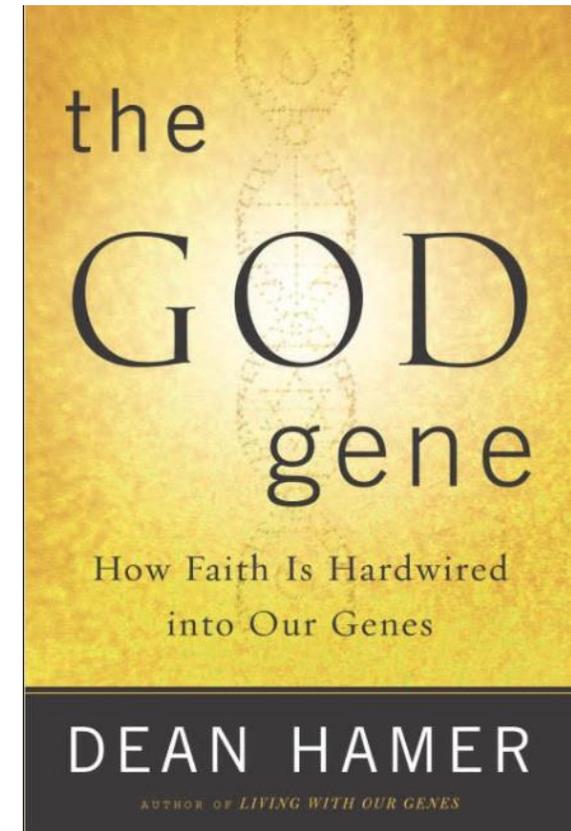
	Genetic	Shared Environment	Non-shared Environment
Retrospective	12%	56%	32%
Current	44%	18%	38%

A God Gene? Story of VMAT2



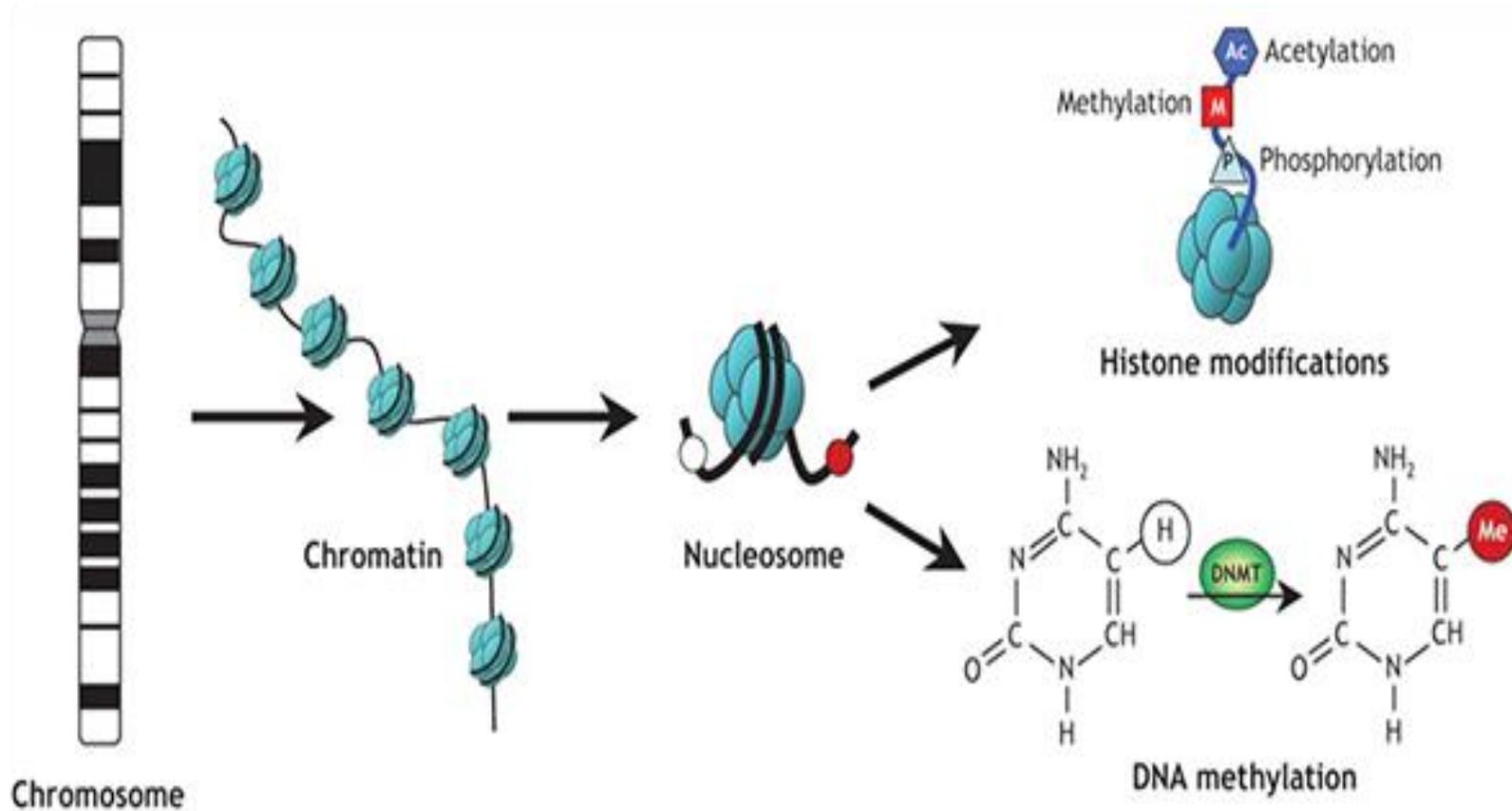
SLC18A2	
Identifiers	
Aliases	SLC18A2, SVAT, SVMT, VAT2, VMAT2, solute carrier family 18 member A2, Vesicular monoamine transporter 2, PKDYS2
External IDs	OMIM: 193001 MGI: 106677 HomoloGene: 2298 GeneCards: SLC18A2
Gene location (Human) [hide]	
<p>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y MT</p>	

Dean Hamer (*The God gene: how faith is hardwired into our genes*) identifies one particular variation, a change from an A to a C, present in 28% of the alleles in his data set, as a marker for the more “spiritual” version of this gene. **This work has not been published in a scientific journal.**



Cocaine users displayed a marked reduction in VMAT2 immunoreactivity as well as reduced [3H]DTBZ binding and dopamine levels. This could play a role in causing disordered mood and motivational processes in more severely dependent patients (Little et al., 2003).

Epigenetic modifications, ON/OFF mechanism

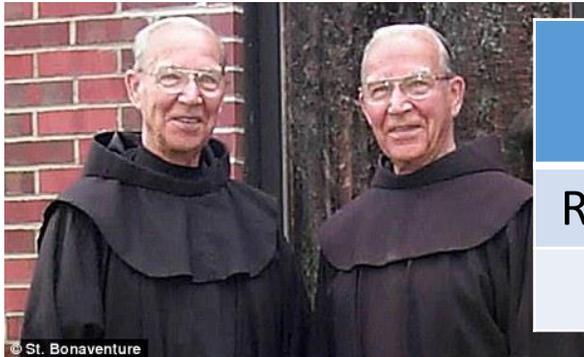


Fly and the maggot have exactly the same gene sequence but look very different.

Genes in our brain do not produce haemoglobin as do red blood cells because they have been scrunched up to stop their expression at a very early stage

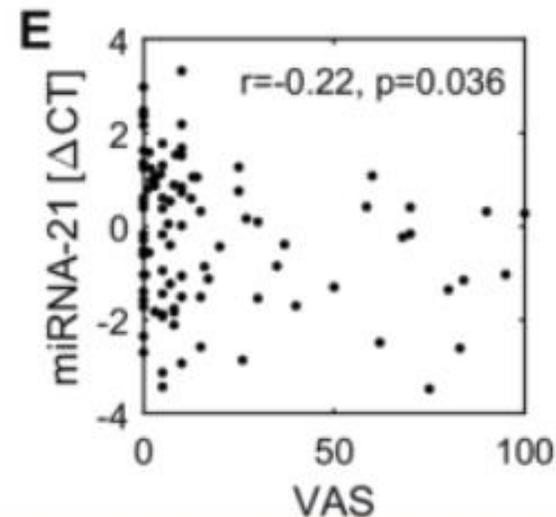
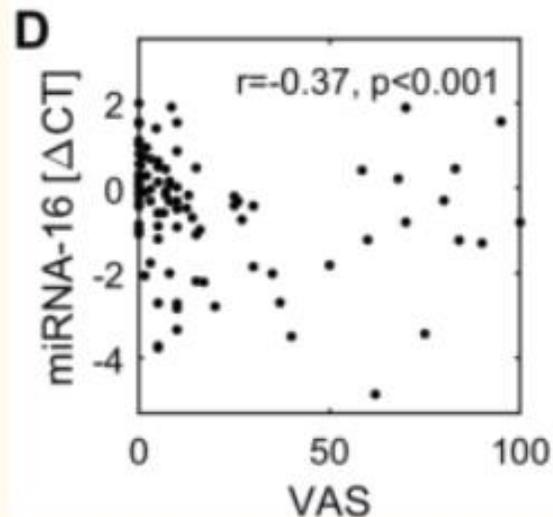
Alcoholics have their gene responsible for alcohol breakdown turned on, so their need increase

Epigenetic modification and spirituality



	Genetic	Shared Environment	Non-shared Environment
Retrospective	12%	56%	32%
Current	44%	18%	38%

Genetic dissimilarity between twins over time indicated that environmental factors are taking over which may be explained through epigenetic modifications



Wiegand et al., 2018 reported stress-associated miRNAs.

- miRNA-21 has been implicated in cellular stress response coping with oxidative stress, which in turn also appears to be a result of perceived psychological stress. Downregulated by sympathetic activation.
- miRNA-16 has been implicated in SERT (serotonin transporter) expression.

Other Psychoneuroimmunology parameters

- Sympathoadrenomedullary (SAM) axis: sympathetic nervous system (SNS); and the hypothalamicpituitary-adrenocortical axis (HPAA).
 - Chemokines
 - Cytokines
 - Neuropeptide hormones
 - Matrix metalloproteinase

Spiritual CAM

- Systematic Review (Hullet et al., 2016)

Table 1. Spiritually Based Interventions and Psychosocial-Spiritual Outcomes in Breast Cancer Survivors.

Study Number (See Table 3)	Spiritually Based Interventions	Psychosocial-Spiritual Outcomes (↓ or ↑) ^a
1,4, 6, 8, 15, 18	CBSM, MBSR, Qigong, RVT, Yoga	↓ Depression
1, 4, 6, 8, 12	CBSM, MBSR, RVT, Yoga	↓ Anxiety
2, 4, 14, 15, 18, 19, 20	MBCR, MBSR, Qigong, Yoga	↑ Quality of life/vitality/vigor
4	Yoga	↓ Distress
4, 17	MBSR, Yoga	↓ Symptoms
2	MBSR	↑ Coping
5, 7	CBSM	↑ Relaxation
1, 6, 8, 12, 14, 18	CBSM, MBCR, MBSR,RVT, Yoga	↓ Stress
16	Tai Chi	↑ Stress
9, 12, 13	MBSR	↑ Mindfulness
11	BMS	↑ Spiritual growth/spiritual well-being
13	MBSR	↓ Rumination
14	MBCR	↑ Social support
15, 17, 18, 19, 20	MBSR, Qigong, Stretching, Yoga	↓ Fatigue
9, 14	MBCR, MBSR	↑ Mood
17	MBSR	↑ Cognitive function (postchemotherapy)

Abbreviations: CBSM, cognitive-based stress management; MBCR, mindfulness-based cancer recovery; MBSR, mindfulness-based stress reduction; RVT, relaxation visualization therapy; BMS, body-mind-spirit.

^a↓ indicates decreased and ↑ indicates increased.

Spiritual CAM and gene expression

• Systematic Review of Gene Expression Changes Induced by Meditation and Related Practices (Buric et al., 2017)

- Overall, the studies indicate that these practices are associated with a downregulation of nuclear factor kappa B pathway; this is the opposite of the effects of chronic stress on gene expression and suggests that MBI practices may lead to a reduced risk of inflammation-related diseases.

Save	Research design	Type of population (experimental group sample size)	Control group type (size)	Meditation or meditation-related type of practice	Practice frequency, training time	Gene expression technology (bioinformatics analysis)	Cell type	Biological outcome	Psychological and other outcomes	
	Li et al. (29)	CS	Experienced practitioners (n = 6)	Naïve (n = 6)	Qigong	60–120 min/day, 1–5 years	Genome-wide: Affymetrix Human Genome U95 (N/A)	Peripheral blood neutrophils	Genes related to: apoptosis– Cell metabolism– Immune regulation+	N/A
	Sharma et al. (30)	CS	Experienced practitioners (n = 42)	Naïve (n = 42)	Sudarshan Kriya (breath regulation)	>60 min/day, at least 1 year	RT-PCR of 9 genes (N/A)	Peripheral blood lymphocytes	Genes related to: oxidative stress ns, DNA damage ns, cell cycle control ns, aging ns, apoptosis+	N/A
	Kumar and Balkrishna (31)	CS	Leukemia patients (n = 8)	Naïve (n = N/A)	Pranayama (breath regulation)	N/A	Genome-wide: Expression Array System of Applied Biosystems (N/A)	Peripheral blood lymphocytes	Genes related to: immune regulation+ Apoptosis+	N/A
	Creswell et al. (32)	LG	Normal older adults (n = 20)	Wait list (n = 20)	Mindfulness-based stress reduction, 8 weeks	30 min/day, 8 weeks	Genome-wide: Illumina HT 12 BeadChip (TELiS, NF-κB)	PBMC	Transcription factors: NF-κB–; Proteins: CRP– IL-6 ns	Loneliness–
	Black et al. (33)	LG	Dementia caregivers (n = 20)	Relaxing music (n = 20)	Kirtan Kriya Meditation	12 min/day, 8 weeks	Genome-wide: Illumina HT 12 BeadChip (TELiS, NF-κB, and IRF)	PBMC	NF-κB–, IRF+ IL-6 ns, IL-8 ns, IL1B ns, TNF ns	Depression–, mental health+

Research gaps; Proposing the question

- Technologies available: fMRI, SPECT, Next-Gen Sequencing, Expression array
- Would genetics and epigenetics variations influence response to spiritual therapy? → *spiritogenomics*
- Confounding factors?