



Meaning in life and biological functioning: A multisystem synthesis and agenda for future research

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ABSTRACT

Meaning in life (MIL) has been reliably linked to healthier aging, lower disease risk, and reduced mortality across large epidemiologic cohorts, yet the biological processes that accompany these associations remain poorly characterized. This Review synthesizes evidence across five systems—genomic, neurobiological, endocrine, autonomic, and inflammatory—to clarify how MIL aligns with patterns of biological functioning. Genomic studies suggest modest heritability and preliminary neural relevance, though specific molecular pathways remain uncertain. Neuroimaging findings indicate that MIL corresponds to features of large-scale network organization, particularly within the insula, default mode network, and limbic circuitry. Endocrine and autonomic studies report associations between MIL and cortisol rhythms, stress recovery, and patterns of sympathetic and parasympathetic activity. Inflammation-related research provides the most consistent evidence, with higher MIL associated with lower chronic inflammatory markers and, in limited cases, indicators of more effective immune functioning. Together, these findings indicate that MIL has been associated with variation in biological markers across multiple systems. Nevertheless, most evidence is cross-sectional, and directionality remains unresolved. Future work using longitudinal, experimental, and intervention-based designs will be essential for determining when, how, and under what conditions MIL is reflected in biological processes.

1. Introduction

Meaning in life (MIL) refers to the extent to which individuals perceive their lives as making sense, directed toward valued goals, and worth living (King and Hicks, 2021). Scholarship in this area has converged on a tripartite model comprising three correlated but distinct dimensions: (1) comprehension (or coherence), the cognitive appraisal that one's life has order and consistency; (2) significance (or mattering), the evaluative judgment that one's life has inherent value, importance, and worth not just to one's self or others, but to the wider world as well; and (3) purpose, the motivational sense of having valued goals and life aims that guide behavior (Martela and Steger, 2016; George and Park, 2016). Although purpose (i.e., purpose in life [PIL]) is theorized to reflect one dimension of a broader sense of MIL, historically it has been used interchangeably with MIL (Brandstätter et al., 2012).

A growing body of large-scale, epidemiologic research has identified MIL and PIL as robust predictors of health and longevity (Czekierda

et al., 2017; Kim et al., 2017). For example, in a meta-analysis of over 136,000 adults, individuals with higher PIL showed a 17% lower risk of cardiovascular events and all-cause mortality over time, compared to those with low PIL, and, in a large, prospective study of over 150,000 participants, it was found that higher MIL was associated with a reduced risk of all-cause mortality of 13% over approximately six years (Cohen et al., 2016; Sutin et al., 2025a). Longitudinal analyses have also shown that greater PIL predicts lower incidence of stroke, myocardial infarction, and metabolic disease, as well as better physical functioning and reduced disability over time (Kim et al., 2013a, 2013b; Hill and Turiano, 2014; Boyle et al., 2010; Hafez et al., 2018).

MIL and PIL has also been prospectively linked to lower risk of cognitive decline and dementia (Sutin et al., 2024a). For example, in a recent longitudinal cohort study of more than 13,000 U.S. adults aged 45 and older, individuals with higher PIL were 28% less likely to develop cognitive impairment compared to those with lower PIL, even after controlling for sociodemographic factors, depressive symptoms, and

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APOE-ε4 carrier status (Howard et al., 2025). Similar findings were seen in a recent meta-analysis (Sutin et al., 2023a) that synthesized data from eight prospective cohort studies including over 200,000 adults. Results indicated that, after controlling for sociodemographic, behavior, and

clinical risk factors, including depressive symptoms and APOE risk status, higher MIL was associated with a 20% reduced risk of developing dementia. Collectively, these findings suggest MIL is an important correlate of long-term health.

Table 1
Search terms.

Domain	Construct terms	Biological terms	Inclusion criteria	Exclusion Criteria	Data of Search	Number of studies identified
Genomics	"meaning in life" OR "purpose in life" OR "life meaning" OR "life purpose" OR "eudaimonic well-being" OR "eudaimonic well being" OR "eudaimon*" OR "eudaemon*")	("genetic" OR "genetics" OR "genomics" OR "genome-wide" OR "genome wide" OR "genome-wide association" OR "GWAS" OR "polygenic" OR "polygenic score" OR "polygenic risk" OR "PRS" OR "heritability" OR "twin study" OR "twin studies" OR "SNP-based heritability" OR "chip heritability" OR "LD score regression" OR "LDSC" OR "genetic correlation" OR "Mendelian randomization" OR "MR" OR "epigenomic" OR "epigenomics" OR "epigenome-wide" OR "EWAS" OR "DNA methylation" OR "methylome" OR "transcriptomic" OR "transcriptomics" OR "gene expression" OR "RNA-seq" OR "RNA sequencing" OR "microarray" OR "proteomic" OR "proteomics" OR "metabolomic" OR "metabolomics" OR "multi-omics" OR "multiomic" OR "systems biology")	human OR humans OR participants	(animal OR animals OR mouse OR mice OR rat OR rodent OR "in vitro" OR religiosity OR spirituality OR "case report" OR "case study" OR "case studies")	June 9th 2026	93
Neurobiology	–	("neurobiology" OR "neural correlates" OR "neuroimaging" OR "fMRI" OR "functional MRI" OR "resting-state" OR "resting state" OR "functional connectivity" OR "connectivity" OR "MRI" OR "structural MRI" OR "cortical thickness" OR "gray matter" OR "grey matter" OR "white matter" OR "PET" OR "positron emission tomography" OR "EEG" OR "ERP" OR "MEG" OR "molecular imaging" OR "neurotransmitter" OR "dopamine" OR "serotonin" OR "default mode network" OR "DMN" OR "salience network" OR "executive control network" OR "frontoparietal" OR "prefrontal cortex" OR "PFC" OR "anterior cingulate" OR "ACC" OR "insula" OR "hippocampus" OR "amygdala" OR "striatum" OR "precuneus" OR "posterior cingulate" OR "PCC" OR "network topology")	–	–		227
HPA axis	–	"HPA axis" OR "hypothalamic pituitary adrenal" OR "cortisol" OR "corticosterone" OR "corticotropin" OR "ACTH" OR "adrenocorticotrophic hormone" OR "CRH" OR "CRF" OR "stress response" OR "stress reactivity" OR "diurnal cortisol" OR "cortisol awakening response" OR "CAR" OR "hair cortisol" OR "salivary cortisol" OR "urinary cortisol"	–	–		15
Autonomic	–	"autonomic nervous system" OR "autonomic regulation" OR "parasympathetic" OR "sympathetic" OR "vagal tone" OR "vagus nerve" OR "baroreflex" OR "heart rate variability" OR "HRV" OR "respiratory sinus arrhythmia" OR "RSA" OR "cardiac vagal" OR "pre-ejection period" OR "electrodermal activity" OR "skin conductance" OR "blood pressure variability"	–	–		33
Inflammatory	–	("inflammation" OR "inflammatory activity" OR "cytokine" OR "cytokines" OR "interleukin" OR "IL-6" OR "IL6" OR "IL-1β" OR "IL1β" OR "tumor necrosis factor" OR "TNF" OR "C-reactive protein" OR "CRP" OR "inflammatory markers" OR "immune system" OR "immune function" OR "immunological" OR "inflammatory response" OR "proinflammatory" OR "anti-inflammatory" OR "neuroinflammation")	–	–		58

There are several ways in which MIL may help to support better overall health. For example, individuals higher in MIL consistently report a range of health behaviors, such as greater physical activity, more consistent use of preventive healthcare, better sleep quality, and lower rates of substance misuse that are associated with health (Kim et al., 2020; Sutin et al., 2025b). MIL has also been linked to better stress management, more frequent use of proactive and problem-focused coping, and enhanced emotional recovery following negative experiences, (Ward et al., 2023; Halama, 2014; Sutin et al., 2024b) all of which may help to support long-term health.

Taken together, the above findings demonstrate MIL is reliably associated with healthier aging, reduced disease risk, and longer survival. Despite these robust associations, however, the biological mechanisms that might explain MIL's relevance for health remain poorly understood. In particular, it remains unclear whether observed associations with biological systems reflect direct biological processes or are driven by behavioral and lifestyle factors.

Prior research has focused largely on psychosocial and behavioral pathways (Hill and Pfund, 2025; Hooker et al., 2018) and, although some reviews have considered biological correlates (e.g., inflammation), (Kim et al., 2019; Ryff and Kim, 2020) these findings have typically been examined within specific systems and have not been evaluated in relation to one another across domains. Clarifying these patterns is essential for determining whether associations between MIL and health are evident across biological domains and how these associations should be interpreted. Accordingly, unlike prior reviews, which have typically focused on individual biological systems or psychosocial pathways, the present review evaluates evidence across genomic, neurobiological, endocrine, autonomic, and inflammatory domains to assess whether the associations between MIL and biological functioning show consistent patterns, while explicitly considering conceptual heterogeneity, behavioral confounding, and differences in study design and measurement.

2. Methods

The current review adopts a critical narrative synthesis approach focused on identifying conceptually informative and mechanistically relevant findings across biological domains. This approach is well-suited to the heterogeneity of measurement strategies and study designs that characterize the literature and allows for synthesis of the available evidence.

Relevant studies were identified through targeted searches in PubMed using a priori Boolean search strings developed separately for each biological domain. Search strings were initially executed in PubMed between November 8th and November 10th, 2025, and searched within "All Fields". These search strings were reviewed on June 9th, 2026. The full Boolean search strings and number of PubMed records returned for each domain are provided in Table 1. Additional studies were located through forward and backward citation searches of key articles in Google Scholar to ensure adequate coverage (Table 2).

Search terms included both "meaning in life" (MIL) and "purpose in life" (PIL) because, as noted, these terms have often been used interchangeably in the empirical literature (Brandstätter et al., 2012). To date, most studies evaluating MIL have either relied on unidimensional measures of overall MIL or have focused specifically on the purpose dimension (i.e., PIL). Accordingly, findings described herein use the terminology employed in the original studies (i.e., MIL or PIL) when referring to specific results. However, because PIL is conceptualized as one dimension of a broader sense of MIL, (Martela and Steger, 2016; George and Park, 2016) findings are also discussed collectively in relation to the broader construct of MIL when synthesizing patterns across studies.

To improve search sensitivity, however, variations of "eudaimonia" were also included because this terminology has historically been used to capture meaning-related constructs (Heintzelman, 2018). However, inclusion remained restricted to studies that directly assessed MIL or PIL

as distinct constructs. Studies that assessed broader or alternative indices of well-being (Diener, 1984; Ryff, 1989) were not included. This approach was used to avoid aggregating multiple interrelated dimensions, which would reduce confidence in determining whether observed associations with biological outcomes were attributable specifically to MIL or PIL.

Titles, abstracts, and keywords were screened for references to MIL, PIL, or related eudaimonic constructs in conjunction with biological correlates. Studies referencing broader psychological well-being were only further evaluated when descriptions of the measures indicated inclusion of MIL- or PIL-related subscales.

Because the literature linking MIL and PIL to biological functioning spans multiple biological systems, includes non-equivalent operationalizations of MIL/PIL, populations, and study designs, a PRISMA-based systematic review was not optimally suited for the aims of the current synthesis. Instead, a structured narrative approach was used to integrate findings across domains while attending to sources of variability that constrain interpretation, including conceptual heterogeneity, behavioral confounding, and differences in study design and measurement.

3. Results

3.1. MIL and Genomics

Twin studies provide the strongest evidence to date that MIL is heritable, (van de Weijer et al., 2022) with genetic factors accounting for approximately 23–53% of individual differences (Jamshidi et al., 2020; Wang et al., 2017; Steger et al., 2011; Wootton et al., 2017; de Vries et al., 2022). Molecular findings, however, remain limited. The only known genome-wide association study (GWAS) of MIL (N = 108,154) by Baselmans and Bartels (2018) (Baselmans and Bartels, 2018) identified two genome-wide significant loci and estimated that common variants account for approximately 6% of the phenotypic variance. Moreover, although these associations have not been replicated, functional annotation analyses identified several genes that were overly expressed in frontal cortical and cerebellar tissue. Although preliminary, this suggests genetic influences on MIL may involve neural systems that support higher-order cognitive and affect processes.

A recent analysis by de Vries et al. (2024) (de Vries et al., 2024) aimed to clarify whether variation in MIL reflects positive functioning or the absence of depressive symptoms, a disorder strongly associated with MIL (Boreham and Schutte, 2023). Using genomic structural equation modeling and GWAS-by-subtraction, the authors generated a "pure" meaning factor (N = 102,300), the portion of MIL variance that was independent of depression. This factor showed a SNP-based heritability of 4.2% and a distinct genetic architecture. Functional annotation highlighted SND1 and LRRC4, genes involved in cell growth and neuronal development, respectively, although no genes or tissues reached genome-wide significance. Notably, once depression-related genetic variance was removed, MIL was no longer associated with psychiatric phenotypes (e.g., loneliness, PTSD) and instead showed nominal positive associations with ADHD, risk-taking, BMI, and current smoking, though none of these survived multiple-testing correction. These patterns, despite being preliminary, suggest MIL may be associated with approach-oriented, motivational, or reward-sensitivity pathways that are obscured when shared internalizing liability is not partitioned out.

While the genetics of MIL is only beginning to emerge, work on epigenetic mechanisms is even more preliminary. In fact, to date, only one large-scale study (N = 1572) has examined the epigenetics of PIL (Kim et al., 2023). In that cohort of older adults, higher MIL was associated with slower epigenetic aging across several second-generation DNA-methylation clocks, although these associations were substantially reduced after adjusting for health behaviors such as smoking, BMI, and physical activity. Transcriptomic evidence is similarly sparse. In a small study of community-dwelling older adults (N = 108), (Cole et al., 2015) higher PIL was associated with down-regulated expression of the

Table 2
Overview of included studies.

Domain	Study	Sample	Design	Construct	Measure	Biological marker / system	Key finding(s)
Genetics	Jamshidi et al., (2020)	Australian twin cohort (TWIN-E); N = 484 MZ pairs, 267 DZ pairs	Twin study	MIL	WHOQOL_6 ¹ : <i>To what extent do you feel your life to be meaningful?</i>	Heritability	0.23 (0.15–0.31)
Genetics	Wang et al., (2017)	British twin cohort (TEDS); N = 354 MZ pairs, 779 DZ pairs	Twin study	MIL	Meaningful Life Measure ²	Heritability	0.52 (0.45–0.58)
Genetics	Steger et al., (2011)	Minnesota Twin Registry; 51 MZ pairs, 40 DZ pairs, 154 unmatched twins	Twin study	MIL	Meaning in Life Questionnaire, (MLQ) ³	Heritability	0.39 (0.19–0.55)
Genetics	Wootton et al., (2017)	TEDS; N = 7102 twins	Twin study	MIL	Meaningful Life Measure ²	Heritability	0.46 (0.40–0.50)
Genetics	De Vries et al., (2022)	Netherlands Twin Register; 2089 MZ pairs, 1939 DZ pairs	Twin study	MIL/PIL	Flourishing scale: <i>I lead a purposeful and meaningful life</i>	Heritability	0.32 (0.25–0.38)
Genetics	Baselmans and Bartels, (2018)	UK Biobank (UKB); N = 108,154	GWAS	MIL	<i>To what extent do you feel your life to be meaningful?</i>	SNP-based heritability	SNP h ² 6.2%; two genome-wide significant loci.
Genetics	De Vries et al., (2022)	UKB; N = 102,300	GWAS-by-Subtraction	“Pure meaning”	Residualized MIL independent of depressive symptoms	SNP-based heritability	SNP h ² = 4.2%; one genome-wide significant SNP identified.
Epigenetics	Kim et al., (2023)	Health and Retirement Study (HRS); N = 1572	Cross-sectional observational study	PIL	7-item PIL subscale of the Ryff Psychological Well-Being Scales ⁴	Biological aging (13 clocks)	PIL inversely associated with biological aging across four clocks (PhenoAge, GrimAge, Zhang epigenetic mortality index, DunedinPoAm), corresponding to 0.25–3 years of slower aging.
Transcriptomics	Cole et al., (2015)	HRS; N = 108	Cross-sectional observational study	PIL	Ryff's PIL scale	Conserved transcriptional response to adversity (CTRA) gene expression profile	Higher PIL was associated with downregulated CTRA gene expression, a profile characterized by lower pro-inflammatory and higher antiviral- and antibody-related gene expression. Associations remained significant after adjustment for demographic and behavioral health factors.
Transcriptomics	Lee et al., (2020)	Korean Adult Longitudinal Study (KALS); N = 152	Cross-sectional observational study	PIL	Ryff's PIL scale	Conserved transcriptional response to adversity (CTRA) gene expression profile	Higher PIL was no longer associated with downregulated CTRA gene expression after controlling for other well-being scales.
Neurobiology	Lewis et al., (2014)	Healthy college adults; N = 70	Cross-sectional structural MRI study	PIL	Ryff's PIL scale	Regional grey-matter volume	Higher PIL associated with greater right insula volume.
Neurobiology	Nair et al., (2024)	Midlife in the United Status (MIDUS); N = 138)	Cross-sectional diffusion MRI study	PIL	Ryff's PIL scale	White matter integrity	Higher PIL was associated with diffusion MRI markers of healthier white matter and hippocampal microstructure.
Neurobiology	Abellana-Perez et al., 2023	Barcelona Brain Health Initiative; N = 624	Cross-sectional resting-state fMRI study	PIL	Ryff's PIL scale	Functional brain connectivity and white matter lesion burden	Higher PIL related to reduced associations between white matter lesion burden and executive functioning; greater connectivity involving default mode network regions
Neurobiology	Mwilambwe-Tshilobo et al., (2019)	Human Connectome Project; N = 970	Cross-sectional resting-state fMRI study	MIL	Meaning and Purpose Survey of the NIH Toolbox on Emotions ⁵	Whole-brain functional network connectivity	Higher MIL was associated with greater connectivity involving default mode and limbic brain networks, as well as greater modular

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Table 2 (continued)

Domain	Study	Sample	Design	Construct	Measure	Biological marker / system	Key finding(s)
Neurobiology	Zhang et al., (2023)	Human Connectome Project; N = 970	Cross-sectional observational neuroimaging study	MIL	Meaning and Purpose Survey of the NIH Toolbox on Emotions ⁵	Global brain connectivity of the right anterior insula	organization of intrinsic brain networks. Higher MIL was associated with lower global connectivity of the right anterior insula, whereas loneliness showed the opposite pattern. MIL also mediated associations between anterior insula connectivity and loneliness.
Neurobiology	Vaccaro et al., (2025)	First-time fathers, pre-post pregnancy; N = 35	Longitudinal resting-state fMRI study	MIL	Personal Meaning Index (PMI) from the Life Attitude Profile-Revised ⁶	Functional connectivity in insular and temporal regions	Higher post-birth MIL was associated with greater increases in functional connectivity involving the insula, temporal pole, and hippocampus.
Neurobiology	Kang et al., (2019)	Overweight adults; N = 177	Cross-sectional fMRI study	PIL	Ryff's PIL scale	Conflict-related neural activity during health decision-making	Higher PIL associated with lower activity in conflict-related brain regions (e.g., anterior insula; lateral prefrontal cortex) during evaluation of self-relevant health messages encouraging physical activity.
Neurobiology	Kang et al., (2022)	College-aged social drinkers' N = 54	fMRI and ecological momentary assessment study	PIL	Ryff's PIL scale	Ventral striatal alcohol cue reactivity	Higher daily PIL attenuated the association between ventral striatal alcohol cue reactivity and subsequent alcohol use following craving.
Neurobiology	Schaefer et al., (2013)	Midlife in the United States (MIDUS) adults; N = 253	Longitudinal study	PIL	Ryff's PIL scale	Eyeblink startle recovery following negative emotional stimuli	Higher PIL was associated with faster emotional recovery, indexed by reduced eyeblink startle responses following negative stimuli.
Endocrine functioning	Rector et al., (2019)	MIDUS adults; N = 513	Cross-sectional observational study	PIL	Ryff's PIL scale	Indices of cortisol (e.g., waking, evening)	Higher PIL was most strongly associated with lower evening cortisol.
Endocrine functioning	Ryff et al., (2006)	Community sample of women; N = 135	Cross-sectional observational study	PIL	Ryff's PIL scale	Diurnal cortisol	Higher PIL associated with lower daily cortisol and flatter daily slope.
Endocrine functioning	Lewis and Hill, (2023)	HRS (N = 6053) and the English Longitudinal Study of Ageing (ELSA); N = 338	Longitudinal cohort study	PIL	Ryff's PIL scale	Allostatic load	Higher PIL associated with lower overall allostatic load over ten years but did not predict rate of change.
Endocrine functioning	Zilioli, et al., (2015)	MIDUS; N = 1054	Longitudinal cohort study	PIL	Ryff's PIL scale	Allostatic load	Higher baseline PIL associated with lower allostatic load 10 years later, even after adjusting for sociodemographic, psychological, and health-related covariates.
Endocrine functioning	Pulopulos and Kozusznik, (2018)	Study 1: healthy adults aged 21–55 years (N = 172); Study 2: healthy adults aged 18–54 years (N = 259)	Cross-sectional observational study	PIL	Life Engagement Test (LET) ⁷ ; Ryff's PIL scale	Diurnal cortisol	In study 1, higher perceived stress was associated with higher diurnal cortisol secretion and flatter diurnal cortisol slopes, but only among people with low PIL.
Endocrine functioning	Fogelman and Canli, (2015)	Community-dwelling older adults; N = 44	Cross-sectional laboratory stress study	PIL	10-item modified version of Ryff's PIL scale	Cortisol stress response and recovery following the Trier Social Stress Test	Higher PIL associated with faster cortisol recovery following acute social stressor; not associated with baseline cortisol or cortisol reactivity.
Autonomic Regulation	Murakami et al. 2025	Healthy young adults; N = 49	Cross-sectional observational study	PIL	Ryff's PIL scale	Heart rate variability	Higher PIL associated with heart rate variability after controlling for sociodemographic characteristics.

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Table 2 (continued)

Domain	Study	Sample	Design	Construct	Measure	Biological marker / system	Key finding(s)
Autonomic Regulation	Sloan et al., (2017)	MIDUS II adults aged 34–83 years; N = 967	Cross-sectional observational study	PIL	Ryff's PIL scale	Resting high-frequency heart rate variability (HF-HRV)	PIL not significantly associated with resting HF-HRV after adjustment for demographic, behavioral, and health covariates.
Autonomic Regulation	Dang et al., (2021)	Healthy young adults; N = 77	Cross-sectional laboratory stress study	MIL	MLQ	Vagally mediated heart rate variability (VmHRV)	MIL demonstrated a quadratic association with resting VmHRV, such that both low and high MIL levels were associated with higher resting VmHRV.
Autonomic Regulation	Ishida and Okada, (2006)	Healthy adults; N = 32	Cross-sectional laboratory stress study	PIL	Purpose in Life Test ⁸	Heart rate variability during stressful laboratory task	Higher PIL was associated with lower sympathetic activation and greater parasympathetic activity during stress induction.
Autonomic Regulation	Ishida et al., (2011)	Healthy adults; N = 89	Cross-sectional laboratory stress study	PIL	Purpose in Life Test ⁸	Heart rate, blood pressure, nose-tip temperature during stressful laboratory task	Higher PIL was associated with lower anxiety and reduced sympathetic nervous system responding during stress induction.
Autonomic Regulation	Beltran-Velasco et al., 2021	Nursing students; N = 45	Cross-sectional laboratory stress study	PIL	LET ⁷	Heart rate variability during simulated clinical emergency	Higher PIL associated with greater HRV during stressful task.
Inflammatory Processes	Sutin et al., 2023	HRS; 8999	Longitudinal cohort study	PIL	Ryff's PIL scale	Immune and inflammatory markers	Higher PIL was associated with lower levels of several immune and inflammatory markers, including neutrophils, CRP, IL–6, and sTNFR1
Inflammatory Processes	Friedman et al., (2007)	Elderly women; N = 135	Cross-sectional observational study	PIL	Ryff's PIL scale	Inflammatory cytokine signaling markers	Higher PIL was associated with lower levels of soluble IL–6 receptor (sIL–6R), even after controlling for sociodemographic and health covariates.
Inflammatory Processes	Lachman and Schiloski, (2024)	MIDUS; N = 1244	Longitudinal cohort study	PIL	Ryff's PIL scale	Composite inflammation index (IL–6, CRP, E-selectin, fibrinogen, ICAM–1)	Higher PIL was associated with lower composite inflammation.
Inflammatory Processes	Friedman and Ryff, (2012)	MIDUS; 998	Cross-sectional observational study	PIL	Ryff's PIL scale	Inflammatory markers	Higher PIL buffered the association between chronic health burden (e.g., autoimmune diseases; cancer) and inflammation, such that individuals with higher PIL exhibited lower levels of inflammation despite greater medical comorbidity.
Inflammatory Processes	Mitchell and Christian, (2019)	Pregnant women; N = 67	Cross-sectional observational study	MIL	MLQ	Serum cytokines (IL–6, IL–4)	Higher MIL was associated with lower IL–6 and showed a positive trend with IL–4. MIL also interacted with SES, such that higher MIL was associated with higher IL–4 among women with high SES.
Inflammatory Processes	Sutin et al., 2025	Adults from 7 cohort studies (HRS, MIDUS, NHATS, ELSA, TILDA, SHARE, HCHS); N = 54,491	Cross-sectional and longitudinal individual-participant meta-analysis	PIL	Various PIL measures, including Ryff's PIL scale	C-reactive protein (CRP)	Meta-analytic findings showed that higher PIL was associated with lower likelihood of persistently elevated CRP and lower risk of developing elevated CRP over time.
Inflammatory Processes	Giannis et al., (2024)	Montreal Health and Aging Study; N = 129, 63–91 years.	6-year longitudinal study with repeated assessments	PIL	LET ⁷	C-reactive protein (CRP)	Within-person, but not between person, increases in PIL were associated with lower CRP levels among adults in early old (approximately 73 years or younger). No such

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Table 2 (continued)

Domain	Study	Sample	Design	Construct	Measure	Biological marker / system	Key finding(s)
Inflammatory Processes	Bower et al., (2003)	Bereaved women; N = 44	Longitudinal bereavement-related disclosure intervention study	MIL			association observed in advanced old age.

Note. NHATS, National Health and Aging Trends Study; TILDA, The Irish Longitudinal study of Ageing; SHARE, Survey of Health, Ageing and Retirement in Europe; HCHS, Hispanic Community Health Study/Study of Latinos.

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conserved transcriptional response to adversity (CTRA), a profile marked by higher pro-inflammatory and lower antiviral- and antibody-related gene expression. This pattern was also seen in an adult Korean sample (N = 152), (Lee et al., 2020) although the association was no longer significant after adjustment for other well-being subscales.

Overall, genomic findings suggest MIL is moderately heritable and polygenic, but specific molecular pathways remain unclear. The small number of genomic studies to date, along with limited replication, few significant loci, and inconsistent functional annotations, makes it difficult to draw firm conclusions, although some signals point toward brain pathways. Building on these tentative patterns, as described in the following section, the neurobiological literature provides a greater level of resolution and begins to localize MIL's associations within identifiable structural and functional brain networks.

3.2. MIL and Neurobiology

A small but growing body of research has examined associations between MIL and both brain structure and functional network organization. For example, structural MRI findings have preliminarily implicated the insula, a cortical region central to interoception, emotional awareness, and self-related processing (Uddin et al., 2017). For example, using data from a small voxel-based morphometry study of healthy adults (N = 70), (Lewis et al., 2014) Lewis et al. (2014) demonstrated that higher levels of PIL were associated with greater right insula grey-matter volume. Although these findings require replication, they raise the possibility that the insula may provide a basis for MIL through the integration of bodily signals, emotional experiences, or self-referential thought.

Other structural work has linked PIL to white-matter integrity and memory-related systems. For example, a diffusion MRI study (N = 138) (Nair et al., 2024) showed that higher levels of PIL were associated with healthier white-matter microstructure and stronger hippocampal pathways, which support learning and memory. Moreover, in a large cohort study of middle-aged adults (N = 624), (Abellana-Pérez et al., 2023) higher PIL was associated with a weaker association between white matter lesion burden and executive functioning, as well as with stronger structural connectivity between default-mode and control-network hubs that support cognitive flexibility. These patterns indicate PIL may be associated with neural integration as adults age and suggests neural integration could partly explain its positive associations with cognitive health. Nevertheless, it is also possible that these associations are reflective of behavioral or lifestyle factors independently linked to both

PIL and neural integrity.

Functional MRI studies have also examined associations between MIL and large-scale brain networks. Using data from the Human Connectome Project, Mwilambwe-Tshilobo et al. (2019) (Mwilambwe-Tshilobo et al., 2019) found that higher MIL corresponded to a more clearly delineated default mode network (DMN), a network involved in autobiographical memory and personal identity. Higher MIL was also associated with connectivity between the DMN and the limbic network, an area integral to emotional processing. In the same cohort, MIL was inversely related to global connectivity of the right anterior insula, whereas loneliness showed the opposite pattern (Zhang et al., 2023). A more selectively integrated insula may therefore support MIL by enabling efficient emotional and social processing.

Preliminary longitudinal evidence indicates that neural organization may shift alongside changes in MIL. For example, in a small study of new fathers (N = 35), (Vaccaro et al., 2025) increases in resting-state connectivity were observed in regions involved in social cognition and emotion, such as the temporal lobes, angular gyrus, thalamus, and insula. Greater increases in insula connectivity predicted higher MIL post-birth, even after accounting for affective responses to the experience of parenting. Although these findings may not generalize to other groups or situations, they raise the idea that, during emotionally-demanding periods, the insula may help integrate socio-emotional experiences into a broader self-concept associated with MIL.

Experimental studies provide some evidence that PIL may be associated with variation in how the brain responds to motivational and emotional challenges. One study (N = 220) has shown that adults higher in PIL show reduced activation of conflict-monitoring and self-regulation regions (e.g., dorsal anterior cingulate cortex) when processing health-related risk messages, suggesting lower regulatory burden (Kang et al., 2019). Daily-level fluctuations of PIL have also been shown to moderate the association between craving-related brain activity in the ventral striatum and alcohol consumption, with particularly heavy drinking occurring on days when individuals (N = 54) reported lower-than-usual PIL (Kang et al., 2022). Finally, in a large study of adults (N = 253), higher PIL has been associated with faster emotional recovery, indexed by reductions in eyeblink startle following negative stimuli, even when PIL was measured two years earlier (Schaefer et al., 2013).

Overall, the available evidence suggests MIL may be associated with several structural and functional systems, including features of the insula, DMN, and limbic regions, as well as regions involved with reward- and conflict-processing. However, most studies are cross-

sectional, underpowered, and limited to specific populations. Larger longitudinal and experimental designs are needed to reliably detect effects, (de Vries et al., 2023) determine whether MIL is linked to neurobiological processes, and clarify whether these associations reflect antecedents, consequences, or bidirectional pathways.

3.3. MIL and Endocrine Functioning

Emerging psychoneuroendocrine evidence suggests MIL is associated with how the hypothalamic–pituitary–adrenal (HPA) axis functions in response to stress. Moreover, although the HPA axis is typically understood as a system mobilized by threat, (Godoy et al., 2018) it is also sensitive to positive psychosocial resources that are associated with regulation, such as supportive social relationships and adaptive psychological characteristics (Hostinar and Gunnar, 2018). Consistent with this, several studies indicate MIL is associated with more favorable patterns of cortisol secretion.

For example, in a study of US adults ($N = 513$), (Rector et al., 2019) higher PIL was correlated with lower evening, but not waking, cortisol, suggesting PIL is associated with a calmer physiologic state. Similarly, in a study of older women ($N = 135$), (Ryff et al., 2006) PIL was associated with diurnal cortisol profiles characterized by lower cortisol across the day and flatter daily slopes, particularly among those aged 75 and older. Findings from large, nationally representative prospective studies (Lewis and Hill, 2023; Zilioli et al., 2015) have also shown that higher baseline PIL is associated with lower allostatic load (an indicator of systemic dysregulation across multiple systems, including the HPA axis) 10 years later, even after controlling for sociodemographic characteristics and other factors associated with bodily wear-and-tear. These findings suggest that reduced multi-system dysregulation could partly account for the relationship between PIL and long-term health.

There is also preliminary evidence that PIL may be associated with differences in how the HPA axis responds to stress. In fact, (Pulopulos and Kozusznik (2018) found partial support for this buffering hypothesis, showing that, in one of two samples ($N = 172$), higher perceived stress was associated with greater total cortisol output and flatter diurnal slopes, but only among individuals low in PIL. Relatedly, a small laboratory study of older adults ($N = 44$) (Fogelman and Canli, 2015) showed that higher PIL was associated with faster cortisol recovery from an induced social stressor, even though it was not associated with baseline or reactivity levels of cortisol. These findings are in line with the idea that purpose and meaning can promote adaptive coping, such as positive reappraisal, (Ward et al., 2023) which are, in turn, linked to more efficient downregulation of physiologic responses.

Overall, current findings demonstrate MIL has been associated with variation in HPA-axis regulation through its relations with cortisol rhythms, systemic dysregulation, and recovery from stress. Nevertheless, the findings largely rely on single-timepoint measurements or variable stress paradigms, making it difficult to identify reliable mechanisms or directionality. Continued insight will require experimental and longitudinal designs with repeated measures to determine whether, and through which pathways, MIL influences HPA-axis functioning and long-term health.

3.4. MIL and Autonomic Regulation

There is some evidence linking MIL with autonomic nervous system (ANS) functioning. For example, one small laboratory study ($N = 49$) (Murakami et al., 2025) found that PIL was positively associated with high-frequency heart rate variability (HF-HRV), which reflects variability in the time between heartbeats and is associated with self-regulatory capacity and health at optimal levels. However, in a large, nationally representative sample of middle-aged adults ($N = 967$), no association between HF-HRV and PIL was detected (Sloan et al., 2017). More complex associations have also been observed with MIL. In fact, (Dang et al. (2021) reported a quadratic association between MIL

and HF-HRV where moderate levels of MIL were associated with lower HF-HRV and both high and low levels associated with higher HF-HRV ($N = 77$). Although this pattern is somewhat counterintuitive and requires replication, it raises the possibility that similar autonomic profiles may reflect different underlying states across the MIL continuum. For example, higher HF-HRV among those low in MIL may be associated with boredom, disengagement, or general under-arousal, whereas higher HF-HRV among those high in MIL may signal behavioral engagement and more efficient emotion regulation.

Preliminary evidence also suggests PIL is associated with autonomic responses to stress. For example, in a small study ($N = 32$) where participants underwent an emotionally-arousing stress induction, individuals low in PIL showed elevated sympathetic activation, inferred through HRV patterns, whereas those high in PIL showed minimal reactivity (Ishida and Okada, 2006). A follow-up study ($N = 59$) showed a similar pattern during a task designed to raise performance anxiety where individuals higher in PIL exhibited smaller increases in heart rate and anxiety, relative to those lower in PIL, even after adjusting for demographic factors (Ishida et al., 2011). Similarly, in a small study of nursing students ($N = 45$) (Beltrán-Velasco et al., 2021) undergoing a simulated emergency situation, higher levels of PIL were associated with greater parasympathetic modulation. Together, these findings tentatively suggest that PIL may be linked to adaptive autonomic functioning by contributing to more regulated parasympathetic activity at rest and by dampening sympathetic reactivity during stress.

Overall, the limited research available suggests MIL may be associated with more adaptive patterns of autonomic regulation, including healthy parasympathetic activity and reduced sympathetic reactivity. However, the findings are inconsistent and based on small samples. Larger studies using standardized measurements and repeated assessments across contexts are necessary to determine whether MIL is reliably associated with autonomic functioning and whether these patterns help account for its associations with long-term health.

3.5. MIL and inflammatory processes

Accumulating psychoneuroimmunology research suggests MIL is associated with variation in immune processes. Although inflammatory activity is classically thought of as a response to infection, tissue damage, or stress, it can also be shaped by positive psychosocial factors. Several studies, to date, have indicated that MIL is associated with variation in levels of circulating inflammatory proteins.

Cross-sectional work has shown inverse associations between MIL and a range of inflammatory markers. For example, in a large study of nearly 9000 adults, (Sutin et al., 2023b) higher PIL was inversely associated with inflammatory cytokines, including IL–6, and similar findings examining PIL have been reported in other independent samples, including other large, nationally representative samples (Friedman et al., 2007; Lachman and Schiloski, 2024). For example, in a large, population based study of adults ($N = 998$), (Friedman and Ryff, 2012) higher PIL buffered the association between chronic disease burden and inflammation, such that individuals with higher PIL had lower levels of IL–6 and CRP despite greater medical comorbidity. Data from a small study of pregnant women ($N = 67$) (Mitchell and Christian, 2019) also suggests MIL may be associated with anti-inflammatory processes, as higher MIL was associated with greater IL–4 among women with higher socioeconomic status (Mitchell and Christian, 2019). Prospective studies further support these associations. Meta-analytic findings have shown that higher PIL is associated with a reduced likelihood of developing elevated CRP up to a decade later, (Sutin et al., 2025b) and within-person analyses have shown that changes in PIL are associated with changes in CRP: in a multi-wave study of older adults ($N = 129$), periods marked by higher-than-normal PIL were characterized by lower levels of CRP (Giannis et al., 2024).

Taken together, these findings suggest MIL is linked to lower pro-inflammatory activity and more efficient immune functioning.

However, the current research base is limited by varying sampling procedures and diffuse inflammatory markers, indicating the need for larger, standardized studies to clarify and confirm the pathways that link MIL and inflammation to long-term health.

4. Discussion

The above findings collectively indicate that higher MIL is associated with patterns of adaptive biological functioning across multiple domains, although the findings are heterogeneous and vary in strength across systems. Genomic findings remain preliminary and indicate modest polygenic contributions with potential neural relevance. Neurobiological studies have reported associations with features of large-scale network organization, particularly within the insula, default mode network, and limbic circuitry. Endocrine and autonomic findings suggest MIL is associated with patterns of stress physiology, characterized by faster recovery following stress. Inflammatory associations with MIL, which appear to be most commonly examined within the literature, suggest MIL is reliably associated with lower chronic inflammation and, in limited cases, anti-inflammatory markers.

4.1. Synthesis across systems

Although these domains have been examined independently, considering them together raises the possibility that MIL may be associated with biological functioning across systems rather than through isolated processes. Neural systems involved in monitoring internal bodily states and evaluating external stressors may be linked to downstream HPA-axis activation, autonomic adjustments, and inflammatory signaling. Similarly, chronic differences in cortisol rhythms or low-grade inflammation may be associated, over time, with neuroplasticity and functional connectivity, particularly in circuits involved in emotion, self-related processing, and regulation. Taken together, these patterns are consistent with the possibility that MIL may be associated a pattern of regulation that spans neural, endocrine, autonomic, and immune pathways.

One way to organize these findings is through existing models that link MIL to self-regulation and stress processes (Hooker et al., 2018; Kim et al., 2019). Prior frameworks propose that MIL shapes how individuals attend to, interpret, and respond to stimuli, including stressors, which may, in turn, be associated with downstream biological processes such as HPA-axis activity, autonomic responses, and inflammation. Relatedly, it has been suggested that PIL in particular may function as a kind of “homeostatic” resource, (Burrow et al., 2024) which helps to stabilize responses to both positive and negative experiences over time. As such, because many of the above studies examined PIL in particular, these associations may primarily reflect processes related to goal-directed behavior, including engagement of self-regulatory and reward-related systems, rather than processes related to the other dimensions of MIL (i.e., coherence and significance/mattering). However, these models remain largely conceptual, and the available data do not establish whether such processes operate consistently across biological systems or whether observed associations reflect coordinated or causal mechanisms.

At the same time, interpreting these potential cross-system associations and organizing frameworks requires careful consideration of alternative explanations. The observed relationships may reflect shared antecedents, such as dispositional characteristics or early life contexts, that shape both meaning-related processes and biological regulation. With the exception of genetics, directionality is also an important consideration within the domains, as biological functioning may influence the capacity to experience or sustain meaning, and associations may reflect reciprocal processes unfolding over time. Moreover, despite the use of construct-specific measures, it remains possible that observed associations reflect broader dimensions of well-being rather than processes specific to MIL or PIL (Kashdan et al., 2024). These possibilities

place important constraints on causal interpretation of the observed associations.

Behavioral pathways in particular represent a central interpretive issue in this literature. MIL and, especially PIL, is consistently associated with health-related behaviors, including physical activity, sleep, and substance use, (Kim et al., 2020; Copeland et al., 2020) which are themselves closely linked to biological functioning across systems. As a result, behavioral processes may underlie or contribute the observed associations. However, the existing studies cannot determine whether behavioral factors account for these associations or whether they simply covary with meaning in life and biological regulation. Overall, the findings of this review are preliminary, and any cross-system patterns or organizing frameworks should be considered with caution.

4.2. Future directions

Although the current evidence suggests MIL has biological relevance, the field is still in an early, exploratory phase. To move toward a more robust understanding, future research will need to employ tools that can clarify how and under what conditions MIL becomes linked to biological processes. Below represent several possible directions for research.

A central next step is to clarify when and how MIL aligns with biological functioning over time. Most studies rely on cross-sectional designs, which make it impossible to determine whether MIL causes biological change, results from it, or both. Repeated-measures designs (e.g., tracking MIL and inflammatory markers over time) would provide the temporal resolution needed to establish directionality. These designs would also allow, for example, researchers to examine whether within-person increases in MIL are followed by improvements in immune functioning or cortisol output. This work is essential for determining whether MIL is associated with changes in biological functioning over time.

It would also be beneficial to ground future work more explicitly in the structure of MIL itself. The tripartite model of MIL (i.e., coherence, purpose, and significance/mattering) (Martela and Steger, 2016; George and Park, 2016) offers a framework for linking distinct facets of MIL to specific biological processes. Coherence, the sense that life is understandable, may align with systems that regulate stress and help integrate emotional, cognitive, and self-related information into a stable narrative. Purpose, as noted, may engage biological systems underlying reward processing and self-regulation. Significance, or the sense that one's life matters to one's self and others, may relate to social and affiliative processes, including immune pathways sensitive to connection and belonging. Anchoring research to these empirically and theoretically grounded components could help determine whether specific facets of MIL exhibit distinct biological signatures, thereby advancing a more precise understanding of MIL.

Finally, intervention studies are needed to determine whether increases in MIL are associated with corresponding changes in biological functioning. To my knowledge, no studies have systematically examined whether meaning-based interventions lead to downstream changes in cortisol, autonomic recovery, or neural network organization. Of course, randomized controlled trials offer the strongest test of causality, but quasi-experimental approaches may offer opportunities to examine how shifts in MIL align with biological changes over time. These studies will want to consider methodological issues such as the duration and intensity of the interventions needed to produce detectable biological changes, the timing of biological and phenotypic assessments, (Graham-Engeland et al., 2018) and whether commonly used biomarkers, such as inflammatory indicators, are sufficiently sensitive to detect physiologic changes associated with shifts in MIL. Examining if changes in MIL contribute to corresponding changes in biological functioning is essential for determining whether MIL supports a biological pathway toward better health.

5. Conclusion

Across genomic, neurobiological, endocrine, autonomic, and immune systems, emerging evidence suggests meaning in life (MIL) and purpose in life (PIL) are associated with patterns of biological functioning. Although these findings point to the idea that MIL is associated with variation across multiple biological systems, the evidence remains preliminary and in need of replication. As the field advances, larger and more rigorous studies will be essential for clarifying whether MIL is reliably associated with biological processes and for determining whether those associations reflect antecedents, consequences, or bidirectional processes relevant to long-term health.

Declaration of Competing Interest

Dr. Fischer has no biomedical financial interests or potential conflicts of interest.

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