



Short Communications

Meaning in life and Parkinson's disease in the UK Biobank

Angelina R. Sutin^{a,*}, Martina Luchetti^a, Yannick Stephan^b, Antonio Terracciano^a^a Florida State University College of Medicine, United States^b Euromov, University of Montpellier, France

ARTICLE INFO

Keywords:

Meaning
Purpose in life
Parkinson's disease
Neurodegenerative

ABSTRACT

Introduction: Meaning in life is an aspect of eudaimonic well-being associated with lower dementia risk. This research examines whether this protective association extends to Parkinson's disease (PD).

Methods: Participants ($N = 153,569$) from the UK Biobank reported on their meaning in life. Cases of PD were identified through health records.

Results: Meaning in life was associated with a 50 % lower likelihood of prevalent PD (OR = 0.68, 95 % CI = 0.59–0.78). Over the 5-year follow-up, meaning was associated with a 35 % lower risk of incident PD (HR = 0.74, 95 % CI = 0.65–0.83), an association robust to sociodemographic characteristics, depression, history of seeking mental health care, smoking, physical activity, and genetic risk and not moderated by age, sex, education, deprivation, or genetic risk.

Conclusions: Meaning in life is associated with lower risk of incident PD, an association independent of other major risk factors and generalizable across sociodemographic groups. Meaning is a promising target of intervention for common neurodegenerative diseases.

1. Introduction

Meaning in life is a critical component of psychological well-being [1] that reflects the feeling that one's life has purpose, coherence, and significance [2]. Meaning in life, particularly its purpose component, is associated with better cognitive health in older adulthood [3]. Among cognitively healthy individuals, for example, those who feel their life is meaningful and purposeful are less likely to develop dementia over up to 17 years of follow up, an association that has replicated in eight independent cohorts [4]. Prior to dementia, meaning in life is likewise associated with better cognitive function [5] and healthier behavioral and clinical profiles [6] that support brain health. Meaning may have similar protective associations with other neurodegenerative disorders, including Parkinson's disease (PD). Using the UK Biobank [7], this study tests the hypothesis that greater feelings of meaning in life are associated with lower risk of developing incident PD. We also examine prevalent PD and whether the association with incident PD is moderated by sociodemographic factors or genetic risk.

2. Method

2.1. Participants and procedure

Participants were from the online mental health assessment administered to UK Biobank participants [7]. From July 2016–July 2017, active participants with a valid email address were invited to complete the online assessment; meaning in life was embedded in this questionnaire [7]. Linked health records from the National Health Service (NHS) were used to identify prevalent and incident cases of PD (see below). The North West Multicenter Research Ethics Committee provided ethical oversight and approval for the UK Biobank. All participants gave informed consent. This research has been conducted using the UK Biobank Resource under Application Number 57672.

2.2. Measures

Meaning in life. Meaning in life was measured with the item, "To what extent do you feel your life to be meaningful?" rated on a 5-point scale from 1 (*not at all*) to 5 (*an extreme amount*). Higher ratings indicated greater feelings of meaning in life.

Parkinson's disease. NHS hospital inpatient records or death records

* Corresponding author at: Florida State University College of Medicine, 1115 W. Call Street, Tallahassee, FL 32306, United States.

E-mail address: angelina.sutin@med.fsu.edu (A.R. Sutin).

were used to identify Parkinson's disease. Data were from the UK Biobank Outcome Adjudication Group (https://biobank.ndph.ox.ac.uk/showcase/showcase/docs/alg_outcome_main.pdf). Cases of PD were the earliest documentation of relevant International Classification of Diseases code or cause-specific death from death register records. Cases of PD prior to the mental health assessment were analyzed as prevalent cases and excluded from the analysis of incident PD; incident cases were cases diagnosed after the assessment of meaning.

Covariates. Sociodemographic covariates were age in years at the measurement of meaning, and sex (0 = female, 1 = male), education (0 = no university degree, 1 = yes university degree), and the Townsend deprivation index [8], and physical activity measured as meeting the threshold of recommended moderate-to-vigorous physical activity based on the International Physical Activity Questionnaire (0 = below threshold, 1 = above threshold) [9] measured at baseline. There was an average of 7.60 years (SD = 0.87; range = 5.88–11.18 years) between the first UK Biobank visit and the measurement of meaning. History of elevated depressive symptoms (0 = never, 1 = ever) was measured as ever surpassing the threshold for severe depressive symptoms at any of the four UK Biobank visits (Patient Health Questionnaire-2 >= 3) [10]. Smoking history was measured as ever smoker across the four visits (0 = never, 1 = ever). Polygenic scores for PD controlled for genetic risk for PD [11]. Concurrent depression and anxiety were measured with items from the Patient Health Questionnaire [12] and the Generalized Anxiety Disorder-7 [13], respectively, and categorized into current distress (at least half the days in the last two weeks; 0 = no, 1 = yes).

2.3. Statistical approach

We tested mean-level differences in meaning in life by prevalence and incidence with a one-way analysis of variance that compared no, prevalent, and incident PD, controlling for age, sex, education, and deprivation. We used logistic regression to predict prevalent versus no PD from meaning, controlling for the covariates. The analysis of incidence used Cox regression to test the association between meaning in life and risk of developing PD. Time to PD was calculated from the date of the mental health assessment to the first date of diagnosis in the records. For participants who did not develop PD, time was censored on October 10, 2021, or date of death for participants who died. Meaning in life was entered as a predictor of PD, controlling for age, sex, education, and deprivation (Model 1). Sensitivity analyses excluded participants who developed PD within two years (Model 1.1) or four years (Model 1.2) of the meaning assessment or participants younger than 60 (Model 1.3). History of depression, smoking, and physical activity were added to Model 1 to test whether the association was accounted for by these factors (Model 2). PGS for PD was further added to account for genetic risk of PD (Model 3). Current depression and anxiety were then added to account for concurrent psychological distress (Model 4). Finally, we tested whether the association between meaning and PD risk was moderated by age, sex, education, deprivation, or PGS by testing the interaction between meaning and each of these characteristics, controlling for the main effects.

3. Results

Descriptive statistics are in Table 1. Across the analytic sample ($N = 153,569$), 260 participants had prevalent PD and 373 participants developed incident PD over the five-year follow-up (764,346 person-years). Controlling for age, sex, education, and deprivation, participants with prevalent PD had lower average meaning in life (estimated marginal mean [EMM] = 3.42, SE = 0.05) than participants without PD (EMM = 3.70, SE = 0.002; $d_{\text{prevalent versus none}} = -0.34, p < .001$). There was no difference in meaning in life between participants with prevalent or incident PD (EMM = 3.49, SE = 0.04; $d_{\text{prevalent versus incident}} = -0.08, ns$). The logistic regression indicated that every 1-point higher meaning in life was associated with an almost 50 % lower likelihood of having

Table 1
Descriptive statistics for all study variables.

Variable	Total (N = 153,569)	Parkinson's disease		
		None (n = 152,936)	Prevalent ² (n = 260)	Incident (n = 373)
Age (years)	64.02 (7.72)	63.99 (7.72)	69.11 (5.77)	70.21 (5.28)
Sex (male)	43.2 % (66291)	53.1 % (65918)	53.8 % (140)	62.5 % (233)
University degree (yes)	45.3 % (69517)	45.3 % (69233)	42.7 % (111)	46.4 % (173)
Deprivation index ¹	-1.71 (2.83)	-1.71 (2.83)	-2.11 (2.56)	-1.98 (2.69)
Meaning in life	3.69 (0.83)	3.69 (0.83)	3.45 (0.83)	3.52 (0.87)
Follow-up (years)	4.98 (0.44)	4.99 (0.42)	-	2.89 (1.42)
Depression (n = 148,603)	4.6 % (6857)	4.6 % (6831)	5.6 % (14)	3.4 % (12)
Smoking (n = 153,286)	42.7 (65490)	42.7 (65245)	37.1 % (96)	39.9 % (149)
Physical activity (n = 153,569)	45.5 % (69941)	45.6 % (69690)	38.8 % (101)	40.2 % (150)
Current depression (n = 153,552)	6.5 % (9961)	6.4 % (9861)	22.7 % (59)	11.0 % (41)
Current anxiety (n = 153,497)	9.3 % (14,351)	9.3 % (14,252)	18.5 % (48)	13.7 % (51)

¹ 0.1% of missing data on the deprivation index was replaced with the mean. ² Prevalent cases are not included in the longitudinal sample.

prevalent PD (odds ratio = 0.68, 95 % confidence interval = 0.59–0.78).

The association between meaning in life and incident PD is in Table 2. Supporting our hypothesis, meaning was associated with lower risk of developing PD over the follow-up: Among participants without PD at baseline, there was a 35 % reduced risk of developing PD for every 1-point higher meaning, controlling for age, sex, education, and deprivation (Model 1). The association was similar when participants who had been diagnosed within two years ($n = 265$ incident PD; HR = 0.74, 95 % CI = 0.65–0.86, $p < .001$; Model 1.1) or four years ($n = 106$ incident PD; HR = 0.75, 95 % CI = 0.60–0.94, $p = .011$; Model 1.2) of the baseline assessment or who were younger than 60 (HR = 0.73, 95 % CI = 0.65–0.83, $p < .001$; Model 1.3) were excluded from the analysis. The association was also the same when history of depression, smoking, and physical activity were included as additional covariates (Model 2), as well as genetic risk for PD (Model 3). The association was also the same when history of seeking treatment from a general practitioner (33.0 %) or psychiatrist (10.3 %) for nerves, anxiety, tension, or depression was included as a covariate instead of history of severe depressive symptoms (HR = 0.74, 95 % CI = 0.65–0.84, $p < .001$ and HR = 0.74, 95 % CI = 0.65–0.84, $p < .001$, respectively). The association was attenuated by 37 %, but remained significant, when current distress was accounted for (Model 4). The association between meaning and risk of incident PD was not moderated by age ($p = .942$), sex ($p = .911$), education ($p = .319$), deprivation ($p = .320$), or genetic risk ($p = .263$).

4. Discussion

Meaning in life is associated with lower risk of incident PD, an association robust to sensitivity analyses and clinical, behavioral, and genetic covariates. This finding is consistent with work on meaning and lower risk for dementia [4] and supports the hypothesis that having a meaningful and purposeful life may be broadly protective of brain health, particularly relatively common neurodegenerative diseases.

Psychological risk factors for incident PD have focused primarily on mood-related factors, such as depression [14] and neuroticism [15]. Meaning in life is an aspect of eudaimonic well-being that is not the opposite end of the continuum from distress [16]. Current feelings of distress, but not history of depression, attenuated but did not account for all the association with incident PD. The association was likewise not due to smoking or physical activity, which are common behavioral

Table 2

Survival analysis predicting risk of incident Parkinson's disease from meaning in life and covariates.

Predictor	Model 1		Model 2		Model 3		Model 4	
	HR (95 % CI)	<i>p</i>	HR (95 % CI)	<i>p</i>	HR (95 % CI)	<i>p</i>	HR (95 % CI)	<i>p</i>
Age	1.14 (1.12–1.17)	<0.001	1.15 (1.12–1.17)	<0.001	1.15 (1.12–1.17)	<0.001	1.15 (1.12–1.17)	<0.001
Sex	1.92 (1.56–2.37)	<0.001	2.08 (1.64–2.64)	<0.001	2.08 (1.64–2.64)	<0.001	2.14 (1.68–2.72)	<0.001
Degree	1.19 (0.97–1.46)	0.100	1.11 (0.88–1.39)	0.384	1.08 (0.86–1.36)	0.499	1.11 (0.88–1.39)	0.381
Deprivation	0.99 (0.96–1.03)	0.761	1.00 (0.96–1.05)	0.878	1.00 (0.96–1.04)	0.967	1.00 (0.96–1.04)	0.884
Depression	–	–	0.96 (0.52–1.76)	0.882	0.96 (0.52–1.77)	0.893	0.67 (0.35–1.26)	0.211
Smoking	–	–	0.74 (0.59–0.93)	0.010	0.74 (0.59–0.94)	0.013	0.73 (0.58–0.92)	0.009
Physical activity	–	–	0.75 (0.60–0.94)	0.011	0.74 (0.59–0.92)	0.008	0.73 (0.58–0.92)	0.006
PD PGS	–	–	–	–	1.45 (1.30–1.62)	<0.001	1.44 (1.29–1.61)	<0.001
Current depression	–	–	–	–	–	–	2.08 (1.32–3.28)	0.002
Current anxiety	–	–	–	–	–	–	1.60 (1.07–2.40)	0.022
Meaning in life	0.74 (0.65–0.83)	<0.001	0.74 (0.65–0.85)	<0.001	0.74 (0.65–0.85)	<0.001	0.82 (0.72–0.95)	0.007

Note. *N* = 153,309 for Model 1. *n* = 127,118 and *n* = 124,471 for Models 2 and 3, respectively, due to missing data.

HR = hazard ratio. CI = confidence interval. PD PGS = polygenic risk score for Parkinson's disease.

factors associated with both meaning [17,18] and PD [14,19]. There may be other mechanisms that explain why meaning in life is protective. Meaning is associated with greater engagement in everyday life, including mental, physical, and cognitive activities [20] that may help protect the brain from neuropathology. Individuals higher in meaning also tend to be more socially integrated [21], which may have neuroprotective effects [22]. The healthier inflammatory profiles associated with meaning [20] may likewise help reduce risk. Future research could help better identify the mechanisms through which meaning is associated with reduced risk of PD.

The association may be due to the disease process (i.e., low meaning could be a prodromal symptom) rather than protective. That is, the neurodegeneration caused by PD may lead to feeling that life has less meaning rather than greater feelings of meaning protect against PD. Indeed, meaning is conceptually and empirically related to symptoms such as apathy and depression [23], non-motor symptoms common in PD [24]. There are, however, reasons to doubt this reverse causality. The association between meaning and incident PD, for example, persisted when participants diagnosed within up to four years were excluded from analysis and when depression was in the model. In addition, if meaning declined as a function of PD, participants with prevalent PD should score lower on meaning. There was, however, no difference in the average levels of meaning between the prevalent and incident groups. Notably, purpose in life, a construct related to meaning, has a small decline before onset of cognitive impairment and a more rapid decline after the onset of impairment [25]. This pattern suggests that a decline in meaning is more likely after disease onset. More research with repeated measures of meaning over a longer follow-up is needed to evaluate both meaning as a longer-term predictor of PD and change in meaning before and after the onset of PD to differentiate meaning as a protective factor versus prodromal changes in meaning leading to PD onset.

The present research suggests that the association between meaning and lower risk of PD is broadly generalizable. That is, similar to dementia [3], the protective association with PD was similar across age, sex, education, and genetic risk. These findings suggest that meaning may not provide extra protection among those most at risk of PD, but its protective association is also not dampened by the presence of other risk factors. As such, it may be a helpful intervention target, especially among those most at risk.

The importance of meaning for PD might not end with diagnosis. For individuals with dementia, greater purpose (a component of meaning) prior to dementia is associated with fewer behavioral symptoms in the last year of life [26]. Similar to dementia, meaning may help slow the progression of clinical symptoms over time. Although not yet tested with longitudinal data, there is cross-sectional evidence that greater feelings of meaning are associated with less apathy among individuals with PD [27]. Qualitative work also points to the importance of deriving meaning and purpose in everyday activities to sustain a better quality of life

with PD [28]. And, similar to purpose [29], meaning could also serve a resilience function, such that it may help limit symptoms of PD, particularly non-motor symptoms, even in the presence of neuropathology. A higher sense of meaning could also help delay the onset of dementia among PD patients.

The present research has several strengths, including the large sample, prospective design, and PD diagnosis from medical records. Limitations include the relatively short follow-up, the single assessment of meaning, and the use of a dataset without racial and ethnic diversity from a high-income country, which may limit generalizability. In addition, the measure of meaning was a single item. Future research could include longer scales, such as the Meaning in Life Questionnaire, and get repeated assessments of it over time. It is of note, however, that previous studies have found that the association between this item and other markers of health and well-being are similar to longer measures of meaning [5,30]. The PGS scores were also associated with only a limited proportion of the heritability of PD and thus do not account for all the genetic risk. The prevalence of depression history was relatively low, which may be because the measure of depressive symptoms was not sensitive enough to detect severe distress. Of note, however, the associations were similar when history of treatment-seeking for mental health was included as a covariate instead of history of depression based on the PHQ. Despite these limitations, this research is the first to show that meaning in life is a prospective predictor of incident PD. Given that meaning can increase through intervention [31], it may be a promising target for reducing PD risk and maintaining quality of life as the disease progresses.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Funding: Research reported in this publication was supported by the National Institute on Aging of the National Institutes of Health under Award Number R01AG074573. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Data sharing: Per UK Biobank policy, authors cannot share UK Biobank data. Data are available by application to the UK Biobank (<https://www.ukbiobank.ac.uk/>). This research has been conducted using the UK Biobank Resource under Application Number 57672.

References

- [1] T. Schnell, H. Krampe, Meaningfulness protects from and crisis of meaning exacerbates general mental distress longitudinally, *BMC Psychiatry* 22 (2022) 285.
- [2] F. Martela, M.F. Steger, The three meanings of meaning in life: distinguishing coherence, purpose, and significance, *J. Positive Psychol.* 11 (2016) 531–545.
- [3] A.R. Sutin, M. Luchetti, A. Terracciano, Sense of purpose in life and healthier cognitive aging, *Trends Cogn. Sci.* 25 (2021) 917–919.
- [4] A.R. Sutin, M. Luchetti, D. Aschwanden, Y. Stephan, A.A. Sesker, A. Terracciano, Sense of meaning and purpose in life and risk of incident dementia: New data and meta-analysis, *Arch. Gerontol. Geriatr.* 105 (2023), 104847.
- [5] A.R. Sutin, M. Luchetti, Y. Stephan, J.E. Strickhouser, A. Terracciano, The association between purpose/meaning in life and verbal fluency and episodic memory: a meta-analysis of >140,000 participants from up to 32 countries, *Int. Psychogeriatr.* 34 (2022) 263–273.
- [6] K. Czekierda, A. Banik, C.L. Park, A. Luszczynska, Meaning in life and physical health: systematic review and meta-analysis, *Health Psychol. Rev.* 11 (2017) 387–418.
- [7] K.A.S. Davis, J.R.I. Coleman, M. Adams, N. Allen, G. Breen, B. Cullen, et al., Mental health in UK Biobank – development, implementation and results from an online questionnaire completed by 157 366 participants: a reanalysis, *Bjpsych Open* 6 (2020) e18.
- [8] P. Townsend, *Poverty in the United Kingdom*, Allen Lane and Penguin Books, London, UK, 1979.
- [9] C.L. Craig, A.L. Marshall, M. Sjöström, A.E. Bauman, M.L. Booth, B.E. Ainsworth, et al., International physical activity questionnaire: 12-country reliability and validity, *Med. Sci. Sports Exerc.* 35 (2003) 1381–1395.
- [10] K. Kroenke, R.L. Spitzer, J.B. Williams, The Patient Health Questionnaire-2: validity of a two-item depression screener, *Med. Care* 41 (2003) 1284.
- [11] D.J. Thompson, D. Wells, S. Selzam, I. Peneva, R. Moore, K. Sharp, et al., UK Biobank release and systematic evaluation of optimised polygenic risk scores for 53 diseases and quantitative traits, *Preprint* (2022), <https://doi.org/10.1101/2022.06.16.22276246>.
- [12] R.L. Spitzer, K. Kroenke, J.B. Williams, Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire, *JAMA* 282 (1999) 1737–1744.
- [13] R.L. Spitzer, K. Kroenke, J.B. Williams, B. Löwe, A brief measure for assessing generalized anxiety disorder: the GAD-7, *Arch. Intern. Med.* 166 (2006) 1092–1097.
- [14] V. Bellou, L. Belbasis, I. Tzoulaki, E. Evangelou, J.P. Ioannidis, Environmental risk factors and Parkinson's disease: an umbrella review of meta-analyses, *Parkinsonism Relat. Disord.* 23 (2016) 1–9.
- [15] A. Terracciano, D. Aschwanden, Y. Stephan, A. Cerasa, L. Passamonti, N. Toschi, et al., Neuroticism and risk of Parkinson's disease: a meta-analysis, *Mov. Disord.* 36 (2021) 1863–1870.
- [16] M.F. Steger, P. Frazier, S. Oishi, M. Kaler, The meaning in life questionnaire: assessing the presence of an search for meaning in life, *J. Counsel Psychol.* 53 (2006) 80–93.
- [17] B. Konkoly Thege, Y.G. Bachner, T. Kushnir, M.S. Kopp, Relationship between meaning in life and smoking status: results of a national representative survey, *Addict. Behav.* 34 (2009) 117–120.
- [18] A.R. Sutin, M. Luchetti, Y. Stephan, A. Terracciano, Meaning in life and accelerometer-measured physical activity: association based on 67,038 UK Biobank participants, *Ment. Health Phys. Act.* 21 (2021), 100412.
- [19] B. Portugal, F. Artaud, I. Degeay, E. Roze, A. Fournier, G. Severi, et al., Association of physical activity and Parkinson disease in women: long-term follow-up of the E3N cohort study, *Neurology* (2023), <https://doi.org/10.1212/WNL.0000000000207424>.
- [20] A. Steptoe, D. Fancourt, Leading a meaningful life at older ages and its relationship with social engagement, prosperity, health, biology, and time use, *PNAS* 116 (2019) 1207–1212.
- [21] A.R. Sutin, M. Luchetti, D. Aschwanden, J.H. Lee, A.A. Sesker, Y. Stephan, et al., Sense of purpose in life and concurrent loneliness and risk of incident loneliness: an individual-participant meta-analysis of 135,227 individuals from 36 samples, *J. Aff. Dis.* 309 (2022) 211–220.
- [22] B.L. Perry, W.R. McConnell, M.E. Coleman, A.R. Roth, S. Peng, L.G. Apostolova, Why the cognitive “fountain of youth” may be upstream: pathways to dementia risk and resilience through social connectedness, *Alzheimers Dement.* 18 (2022) 934–941.
- [23] X. Glaw, A. Kable, M. Hazelton, K. Inder, Meaning in life and meaning of life in mental health care: an integrative literature review, *Issues Ment. Health Nurs.* 38 (2017) 243–252.
- [24] P. Macías-García, R. Rashid-López, Á. Cruz-Gómez, E. Lozano-Soto, F. Sanmartino, R. Espinosa-Rosso, et al., Neuropsychiatric symptoms in clinically defined Parkinson's disease: an updated review of literature, *Behav. Neurol.* 2022 (2022) 1213393.
- [25] A.R. Sutin, M. Luchetti, Y. Stephan, A. Terracciano, Change in purpose in life before and after onset of cognitive impairment, *JAMA Netw. Open* 6 (2023) e2333489.
- [26] A.R. Sutin, M. Luchetti, Y. Stephan, A. Terracciano, Self-reported sense of purpose in life and proxy-reported behavioral and psychological symptoms of dementia in the last year of life, *Aging Ment. Health* 26 (2022) 1693–1698.
- [27] B. McDaniels, B. Lee, S. Rumrill, K. Edereka-Great, I. Subramanian, The relationship between meaning in life and apathy in people with Parkinson's disease: a cross-sectional analysis, *Aging Clin. Exp. Res.* 35 (2023) 91–99.
- [28] C.M. Whitney, Maintaining the square. How older adults with Parkinson's disease sustain quality in their lives, *J. Gerontol. Nurs.* 30 (2004) 28–35.
- [29] P.A. Boyle, A.S. Buchman, R.S. Wilson, L. Yu, J.A. Schneider, D.A. Bennett, Effect of purpose in life on the relation between Alzheimer disease pathologic changes on cognitive function in advanced age, *Arch. Gen. Psychiatry* 69 (2012) 499–505.
- [30] A.R. Sutin, M. Luchetti, Y. Stephan, A.A. Sesker, A. Terracciano, Purpose in life and stress: An individual-participant meta-analysis of 16 samples, *J. Aff. Dis.* 345 (2024) 378–385.
- [31] C.L. Park, J.E. Pustejovsky, K. Trevino, A.C. Sherman, C. Esposito, M. Berendsen, et al., Effects of psychosocial interventions on meaning and purpose in adults with cancer: a systematic review and meta-analysis, *Cancer* 125 (2019) 2383–2393.