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Assessment of 3-dimensional wisdom in schizophrenia: Associations with neuropsychological functions and physical and mental health



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ABSTRACT

Recent decades have seen growing empirical research in wisdom as a complex, trait-based psychological characteristic. Wisdom has been shown to possess individual and societal benefits through associations with health and wellbeing, but it has not yet been evaluated in people with schizophrenia (PwS). In the current study, we administered a widely used, validated 3-dimensional wisdom scale that includes three interrelated dimensions: cognitive, reflective, and affective. We examined group differences in wisdom, as well as relationships between wisdom and sociodemographics, clinical symptoms, neurocognitive and functional performance, and mental and physical health in 65 stable adult outpatients with chronic schizophrenia or schizoaffective disorder and 96 non-psychiatric comparison participants (NPCPs). Results showed that PwS had lower wisdom scores than NPCPs and that wisdom moderated relationships between diagnostic group and neurocognitive and functional performance; PwS with higher levels of wisdom demonstrated better cognitive performance than did PwS with lower levels of wisdom. In addition, wisdom was positively correlated with performances on multiple neurocognitive tasks in PwS, but not in NPCPs. Finally, reflective wisdom - representing accurate/unbiased introspection and perspective-taking - correlated with all mental health variables in PwS. Our results were limited by a cross-sectional design, but suggest that wisdom, especially reflective wisdom, may be associated with better cognitive performance and better physical and mental health in PwS. It is conceivable that interventions to enhance wisdom may have broad cognitive and mental and physical health benefits in individuals with chronic psychotic disorders.

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1. Introduction

Wisdom has been a subject of philosophical inquiry and religious writings for millennia (Jeste and Vahia, 2008), but empirical research began only in the 1970s, with recent emerging interest in relationships between wisdom and health/well-being (Jeste and Lee, in press). Clayton and Birren (1980) and Ardelt (2003) conceptualized wisdom as consisting of three distinct but interrelated dimensions – cognitive (a deep understanding of human existence and relationships), reflective (accurate/unbiased introspection and perspective-taking), and affective (an emotional affinity for others). Wisdom is often considered to be a trait-based psychological characteristic (Ardelt, 2003) that may increase with age (Worthy et al., 2011), and it has far-reaching benefits to physical (Ardelt, 2000) and mental health (Ardelt, 2003; Thomas et al., 2017), such as subjective well-being (Ardelt and Jeste, 2016; Etezadi

and Pushkar, 2013), life satisfaction (Ardelt, 1997; Ferrari et al., 2011; Zacher et al., 2013), and resilience (Roháriková et al., 2013; Thomas et al., 2017). Importantly, wisdom also mitigates the negative impact of psychosocial distress on mental health and well-being (Ardelt and Jeste, 2016), suggesting that it may serve as a protective factor in individuals coping with adversity.

Despite the importance of wisdom to mental health, there is little research on wisdom in individuals with psychiatric disorders (Khan and Ferrari, 2018), and, to our knowledge, no published studies to date in people with schizophrenia (PwS). Schizophrenia is a serious mental illness characterized by severe disturbances in cognition, insight, emotional control, and social decision making, all of which could impact wisdom. Therefore, PwS would be expected to have lower cognitive, reflective, and affective components of wisdom assessed by the 3-Dimensional Wisdom Scale (3D-WS; Ardelt, 2003), when compared to healthy people. Moreover, aspects of psychotic illness (e.g., duration and severity of positive, negative, and cognitive symptoms) could have a direct impact on components of wisdom (e.g., perspective taking, empathy; Green et al., 2015). Given the putative link between schizophrenia and wisdom, interventions to enhance wisdom may have

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important clinical implications for PwS. Specifically, this approach is consistent with the movement toward patient-centered treatment in PwS, targeting holistic well-being and community functioning rather than symptom reduction exclusively. Indeed, emphasizing positive psychiatry and focusing on resilience building to improve functioning leads to better overall outcomes compared to a traditional deficit-based approach (Farkas, 2007; Jeste et al., 2017; Kane et al., 2015).

Despite the lack of literature on wisdom in PwS, there is a wealth of evidence on the related construct of social cognition in PwS. Social cognition shares neurobiological underpinnings with wisdom (Green et al., 2015; Jeste and Lee, in press) and includes dimensions such as emotion regulation, theory of mind, and prosocial attitudes, which are common components of wisdom frameworks (Bangen et al., 2013; Jeste and Lee, in press). That is, wisdom and social cognition are overlapping but independent psychological constructs. Importantly, emotion regulation (Horan et al., 2013; Strauss et al., 2013) and empathy (Benedetti et al., 2009; Savla et al., 2013; Smith et al., 2012) are lower in PwS than in comparison groups, and these social cognitive deficits have significant functional implications (Green et al., 2015). For example, both Fett et al. (2011) and Smith et al. (2012) reported that increased empathy was associated with better community functioning in PwS.

The importance of functional status in PwS cannot be understated. In addition to social cognitive deficits, neurocognitive performance is consistently and significantly impaired in severe mental illness (González-Pablos et al., 2018; Schaefer et al., 2013; Thompson et al., 2013), and these deficits predict multiple relevant functional outcomes, including quality of life (Mohamed et al., 2008), social problem solving (Green et al., 2000), occupational and economic capacity (Keefe and Harvey, 2012), community functioning (Green et al., 2004), interpersonal interactions (Milev et al., 2005), and instrumental skills (Green et al., 2000). Consequently, it is well established that neuropsychological performance is a crucial endpoint in PwS, and cognition is a prime target for interventions in this population (Keefe and Harvey, 2012).

In the current study, we sought to examine relationships between wisdom and sociodemographics, clinical symptoms, neurocognitive and functional performance, and mental and physical health in PwS. We tested this overall aim with two data-driven hypotheses and two exploratory analyses. Extrapolating from prior literature suggesting the presence of impairments in PwS in social and other aspects of cognition, self-reflection or insight, control over emotions, and social decision making, we first hypothesized that PwS would have lower levels of wisdom than non-psychiatric comparison participants (NPCPs). Our second hypothesis was spurred by reports on wisdom as a protective factor against negative outcomes in healthy older adults (Lee et al., 2018a, 2018b), as well as evidence for related psychological constructs [e.g., happiness (Palmer et al., 2014) and resilience (Lee et al., 2018b)] mitigating the impact of adverse life events in PwS (Johnson et al., 2010; Kukla et al., 2014; Lee et al., 2018b; Palmer et al., 2014). We hypothesized that wisdom would moderate relationships between diagnostic group and neurocognitive and functional performance such that PwS with higher levels of wisdom would show better cognitive and functional performance than would PwS with lower levels of wisdom.

In addition to testing our a priori hypotheses, we also conducted two exploratory analyses. First, we tested overall linear relationships between wisdom dimensions and sociodemographic variables, mental health, and cognitive and functional performance, separately in PwS and NPCPs. Second, we compared PwS who were high in wisdom to PwS who were lower in wisdom, with the goal of identifying dependent variables that differentiated between the groups.

2. Methods

2.1. Study participants and measures

Participants were 65 stable outpatients with chronic schizophrenia/schizoaffective disorder, diagnosed with the Structured Clinical

Interview for the DSM-IV-TR (First et al., 2002), and 96 age- and sex-comparable NPCPs (see Table 1 for demographic characteristics). NPCPs were excluded if they met criteria for a past or present major neuropsychiatric illness, assessed with the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998). Additional exclusion criteria for both groups were as follows: 1) other current DSM-IV-TR Axis I diagnoses, 2) alcohol or other non-tobacco substance abuse or dependence within 3 prior months, 3) diagnosis of dementia, intellectual disability, or a major neurological disorder, or 4) medical disability affecting the capacity to complete study procedures.

Study participants were 23–71 years old and were enrolled in an ongoing study of aging in schizophrenia. Recruitment took place in the greater San Diego area via outpatient clinical and residential referral networks as well as advertisements. The detailed methods of the overall study design have been reported previously (Hong et al., 2017; Lee et al., 2016). Only participants who completed the 3D-WS were included in the current analyses. The study protocol was approved by the UC San Diego Human Research Protections Program and all participants provided written informed consent prior to study procedures. All measures are described in Table 2.

2.2. Statistical analyses

All data analyses were performed using SPSS version 24.0. Continuous variables were assessed for distributional characteristics – positively skewed variables were normalized using a logarithmic transformation and negatively skewed variables were reverse-scored and then log transformed. Greater than 90% of the data were available in PwS and >95% of the data were present in all NPCPs (Table 1). Because wisdom has not been studied in PwS, we sought to minimize the probability of Type II errors (also see Rothman, 1990; Streiner and Norman, 2011), and set the criterion for statistical significance at p < .05 (as opposed to a more conservative cutoff that would decrease statistical power). Given our moderate sample size of 161, it is possible that clinically-relevant group differences would be non-significant despite noteworthy underlying effects.

With respect to the first hypothesis, independent sample t-tests or chi-square tests assessed diagnostic group differences in 3D-WS subscales, as well as group differences in sociodemographic factors, clinical characteristics, subscales, neurocognitive and functional performance, and mental and physical health. To test the second hypothesis, we performed multiple linear regression models, predicting cognitive and functional variables of interest using diagnostic group (PwS and NPCPs), 3D-WS Total Score, and the diagnostic group X 3D-WS Total Score interaction. As a follow-up probe of statistically significant interaction terms, we implemented floodlight analysis (Spiller et al., 2013), also known as the Johnson-Newman (J-N) technique (Johnson and Neyman, 1936), which reveals the specific portions of the moderator's (3D-WS Total Score) distribution where the predictor (diagnostic group) does and does not impact the outcome of interest (in this case, neurocognitive and functional performance). This analysis is considered state-of-the art with respect to interpreting a significant interaction effect because it probes the full range of moderator variables rather than using arbitrary cutpoints, (e.g., 16th, 50th, and 84th percentile; Hayes,

In the first exploratory analysis, we conducted within-group Pearson correlation coefficients to identify significant relationships between variables of interest. We examined scatterplots in order to rule out undue influence from non-linearity and outliers; no such problematic cases were identified. To constrain the overall number of statistical tests conducted, we elected to analyze composite cognitive scores rather than individual subtest scores. Specifically, speeded motor tests (D-KEFS Trails: Visual Scanning, Number Sequencing, Letter Sequencing, Motor Speed; D-KEFS CWIT: Color Naming, Word Reading) and higher-level measures (D-KEFS Trails: Letter-Number Sequencing; D-KEFS CWIT: Inhibition, Inhibition/Switching; phonemic fluency) were

Table 1Group differences across sociodemographic, clinical, cognitive, functional, and mental/physical health variables.

Sociodemographic variables	PwS $(n = 65)$ Mean/% (SD)	NPCP (n = 96) Mean/% (SD)	t or χ^2	d	lf	<i>p</i> -Value	Cohen's
Age, years	51.0 (10.6)	51.3 (10.0)	0.18	1	59	.860	_
Education, years	12.2 (2.5)	14.6 (2.1)	6.64	1	59	<.001	1.05
Sex: % Female	52.3	45.8	0.65	1		.420	_
Race: % White	47.7	64.6	4.53	1		.033	_
Ethnicity: % Non-Hispanic	80.0	83.3	2.09	2		.353	
Relationship status: % in a relationship	7.7	33.3	14.40	1		<.001	
Living situation: % living alone	9.2	20.8	4.13	1		.042	
Clinical variables	PwS	NPCP	t	df		<i>p</i> -Value	Cohen's
	Mean/% (SD)	Mean/% (SD)					
SAPS (positive symptoms)	6.29 (4.29)	0.24 (0.68)	13.60	159		<.001	1.97
SANS (negative symptoms)	5.89 (3.84)	1.01 (1.80)	10.83	159		<.001	1.63
Duration of illness (years)	27.07 (12.70)	_	-	-		_	-
Antipsychotic dose (mg/day) ^b	1.41 (0.83)	-	-	_		-	-
Atypical antipsychotics only	69.2%	_					
Typical antipsychotics only	6.2%	_					
Both	10.8%	_					
Missing data	13.8%	_					
Neurocognitive and functional performand	ce	PwS	NPCP	t	df	<i>p</i> -Value	Cohen's
F		Mean/% (SD)	Mean/% (SD)			P	
D-KEFS Trails Visual Scanning ^a		28.13 (8.62)	18.02 (3.82)	9.93	106.97	<.001	1.52
D-KEFS Trails Number Sequencing ^a		53.17 (28.14)	28.80 (11.51)	8.39	102.25	<.001	1.13
D-KEFS Trails Letter Sequencing ^a		68.13 (41.98)	28.01 (9.01)	9.48	85.76	<.001	1.32
D-KEFS Trails Letter-Number Sequencing ^a		154.44 (75.26)	72.04 (29.81)	10.34	114.58	<.001	1.44
D-KEFS Trails Motor Speed ^a D-KEFS CWIT Color Naming ^a		40.89 (27.17)	23.25 (6.48)	9.47	101.43	<.001	0.89
		35.98 (19.61)	29.08 (6.54)	7.29	157	<.001	0.47
D-KEFS CWIT Word Reading ^a		24.06 (17.21)	21.67 (4.50)	5.11	157	<.01	0.19
D-KEFS Color-Word Interference – Inhibit	ion ^a	77.14 (37.14)	51.79 (14.64)	8.06	114.06	<.001	0.90
D-KEFS CWIT Color-Word Interference – I	nhibition/Switching ^a	87.42 (40.77)	58.69 (15.86)	8.12	106.53	<.001	0.93
Phonemic Fluency		30.95 (12.48)	42.37 (12.99)	5.41	151	<.001	0.90
UPSA-Brief Total Score		70.00 (16.47)	85.01 (9.88)	6.55	93.30	<.001	1.11
Mental health, psychological traits, and qu	ality of life	PwS	NPCP	t	df	<i>p</i> -Value	Cohen's
		Mean/% (SD)	Mean/% (SD)				
Mental well-being (SF-36 Mental Component Scale)		45.61 (10.89)	54.53 (6.51)	4.53	99.11	<.001	0.99
Anxiety (BSI-AS) ^a		7.27 (6.02)	1.24 (1.82)	7.95	97.76	<.001	1.36
Depression (Calgary Depression Scale Tota	al Score) ^a	3.41 (3.75)	0.78 (1.95)	6.66	104.48	<.001	0.88
Perceived Stress		18.27 (6.91)	11.08 (5.86)	7.07	158	<.001	1.12
Life Events		5.43 (5.479)	3.23 (3.342)	2.856	92.37	.005	0.48
Satisfaction with Life		20.28 (7.45)	23.62 (7.23)	2.82	158	.005	0.45
Happiness (CESD) CES-D Happiness Scale	l	7.78 (3.45)	10.67 (2.20)	6.13	119.03	<.001	1.00
Resilience (CD-RISC) Connor Davidson Resilience 10-item Scale Optimism (LOT-R)		23.42 (8.54) 19.53 (3.61)	32.55 (6.02) 23.68 (4.47)	7.40 6.19	104.71 158	<.001 <.001	1.24 1.02
optimizin (bot N)		.5.55 (5.01)	25.00 (1.17)			001	1.02
Physical health	PwS Mean/% (SD)	NPCP Mean/% (SD	t	d	lf	<i>p</i> -Value	Cohen's
SF-36 Physical Component Scale	62.66 (29.25)	87.81 (21.0	,		58	<.001	0.99
Physical co-morbidities (CIRS total score)	8.14 (5.42)	2.80 (3.01)	7.45	1	59	<.001	1.22

Note. Higher scores represent more of the characteristic being measured (depression, resilience, etc.). Higher scores on D-KEFS measures reflect worse performance (more time to completion).

BSI-AS = Brief Symptom Inventory-Anxiety Scale; CES-D = Center For Epidemiologic Studies-Depression; CIRS = Cumulative Illness Ratings Scale; CWIT = Color-Word Interference Test; D-KEFS = Delis-Kaplan Executive Function System; LOT-R = Life Orientation Test-Revised; NPCP = non-psychiatric comparison participants; PwS = people with schizophrenia; SF-36 = Short Form Health Survey; SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; UPSA = UCSD Performance-Based Assessment.

consolidated into domain scores (Processing Speed Composite and Executive Functioning Composite, respectively). Raw scores were transformed into z-scores, which were averaged within each domain to create the overall composite score. Finally, in the second exploratory analysis, we compared PwS in the upper tertile (i.e., \geq 67th percentile; n=19) on 3D-WS total scores (>3.15) to those who were in the bottom two tertiles (n=46) using independent t-tests.

3. Results

Group sociodemographic differences included education, race, relationship status, and living situation; NPCPs had greater educational

attainment, a higher proportion of White participants, were more likely to be coupled, and were less likely to live alone compared to PwS (Table 1). Consequently, education, race, relationship status, and living situation were added as covariates to all subsequent group analyses. Results did not differ when controlling for these variables and we elected to present the unadjusted parameters for ease of interpretation. In terms of the PwS group, risperidone (15.4%), clozapine (15.4%), olanzapine (13.8%), and aripiprazole (13.8%) were the most commonly reported antipsychotic medications. In addition, antipsychotic dosage did not correlate significantly with 3D-WS subscale scores in PwS (r's < 0.24).

With respect to hypothesis 1, PwS had lower scores than NPCPs on the 3D-WS subscales (Fig. 1), as well as neurocognitive and functional

^a Inferential tests were performed on transformed data due to non-normality of the raw values.

b Antipsychotic medication daily dosages were converted to WHO average daily doses based on published standards (WHO, 2009; WHO, 2013).

Table 2Measures.

Test	Example items or ability measured	Citation
Wisdom		
Three-Dimensional Wisdom Scale		Ardelt, 2003
Cognitive wisdom	"Ignorance is bliss"	
D. Carting and allow	"There is only one right way to do something"	
Reflective wisdom	"Things often go wrong for me by no fault of my own"	
	"I try to look at everybody's side of a disagreement	
	before I make a decision"	
Affective (compassionate) wisdom	"If I see people in need, I try to help them one way	
(or another" "It's not really my problem if others are	
	in trouble and need help"	
Neurocognitive and functional performance		
The Delis-Kaplan Executive Functioning System		Delis et al., 2001
Trail Making Test	Simple attention, processing speed, and set shifting	
Color-Word Interference Test	Simple attention, processing speed, and inhibition	
Phonemic Fluency	Language and executive functioning	Benton et al., 1994
UCSD Performance-Based Assessment-Brief	Role-play scenarios measure communication and	Mausbach et al., 2006;
	financial skills	Patterson et al., 2001
Mental health, psychological traits, and quality of life		
Scale for the Assessment of Positive Symptoms		Andreasen, 1983; Andreasen, 1984
Scale for the Assessment of Negative Symptoms		Andreasen, 1983; Andreasen, 1984
Short Form 36 Mental Component Scale		Ware and Sherbourne, 1992
Calgary Depression Scale Brief Symptom Inventory-Anxiety Scale		Addington et al., 1993 Derogatis and Melisaratos, 1983
Life Events Scale		Wethington, 2016
Perceived Stress Scale		Cohen, 1994
Center for Epidemiologic Studies-Depression Happiness Scale		Radloff, 1977
Satisfaction with Life Scale		Diener and Emmons, 1985
Connor-Davidson Resilience 10-item Scale		Campbell-Sills and Stein, 2007
Life Orientation Test-Revised		Chang and McBride-Chang, 1996
Physical health		
Short Form 36 Physical Component Scale		Ware and Sherbourne, 1992
Cumulative Illness Rating Scale		Linn et al., 1968

tests, and mental and physical health measures, with medium to large effect sizes (Table 1). Partially consistent with hypothesis 2, the 3D-WS Total Score moderated the relationships between a) diagnostic group and b) 3/5 D-KEFS Trails tests (Visual Scanning, Number Sequencing, Letter Sequencing), as well as the UPSA-B Total Score (but not the D-KEFS CWIT or Processing Speed/Executive Functioning composite scores). Regression coefficients for this analysis are presented in Table 3 and representative moderation effects are presented in Fig. 2. In each case, PwS with higher levels of wisdom performed similarly to

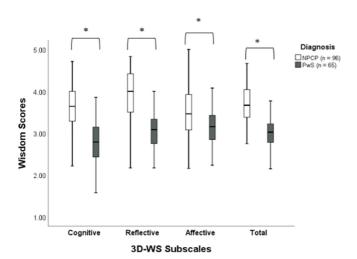


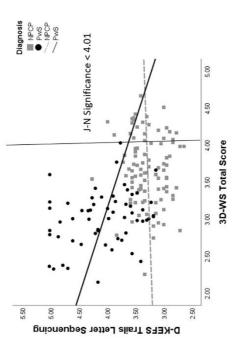
Fig. 1. Boxplots displaying group differences in 3D-WS Scale. *p < .001. Cognitive: t(153) = 9.33; Reflective: t(155) = 7.88; Affective: t(155) = 4.58; Total: t(151) = 9.38 3D-WS = 3-Dimensional Wisdom Scale; NPCP = non-psychiatric comparison participants; PwS = people with schizophrenia.

NPCPs on cognitive and functional tasks, whereas those with lower levels of wisdom scored significantly worse than NPCPs on the same tasks. The J-N region of significance in 3D-WS Total Score ranged from <3.72–<4.15, suggesting that PwS with 3D-WS Total scores less than approximately 3.72–4.15 performed significantly worse than NPCPs with

Table 3Multiple linear regression models

	В	SE B	t	р
1. D-KEFS Trail Making Test-	-Visual Scanning			
Constant	2.60	0.19	13.46	<.001
Diagnostic Group (A)	1.13	0.32	3.55	<.00
Wisdom Total Score (B)	0.07	0.05	1.37	.172
A × B Interaction Term	-0.22	0.10	2.26	.025
2. D-KEFS Trail Making Test-	-Number Sequer	ncing		
Constant	3.18	0.30	10.64	<.00
Diagnostic Group (A)	1.52	0.49	3.08	.003
Wisdom Total Score (B)	0.033	0.08	0.41	.681
A × B Interaction Term	-0.32	0.15	2.07	.041
3. D-KEFS Trail Making Test-	-Letter Sequenci	ng		
Constant	3.11	0.35	8.97	<.00
Diagnostic Group (A)	2.21	0.57	3.86	<.00
Wisdom Total Score (B)	0.05	0.09	0.49	.626
A × B Interaction Term	-0.47	0.18	2.64	.009
4. UPSA Total Score				
Constant	84.11	9.93	8.47	<.00
Diagnostic Group (A)	-44.38	16.39	2.71	.008
Wisdom Total Score (B)	0.25	2.68	0.09	.926
A × B Interaction Term	10.01	5.06	1.98	.0499

Note: Model 1 $R^2=443$; ΔR^2 (A × B) = 0.019; Model 2 $R^2=0.373$; ΔR^2 (A × B) = 0.018; Model 3 $R^2=0.467$; ΔR^2 (A × B) = 0.025; Model 4 $R^2=0.279$; ΔR^2 (A × B) = 0.019. D-KEFS = Delis-Kaplan Executive Function System; UPSA = UCSD Performance-Based Assessment.



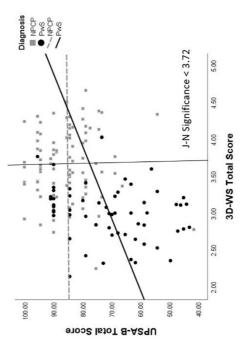


Fig. 2. Results of select moderation analyses. Johnson-Newman (J-N) significance shows where in the distribution of the moderator the two groups differ on the dependent variables of interest. n = 152 for both analyses. 3D-WS = 3-Dimensional Wisdom Scale; D-KEFS = Delis-Kaplan Executive Functioning System, NPCP = non-psychiatric comparison participants; PwS = people with schizophrenia, UPSA-B = UCSD Performance-Based Assessment-Brief

respect to general cognitive status, processing speed, and functional performance.

Regarding the first exploratory analysis, age and education were unrelated to 3D-WS subscale scores, with the exception of a positive correlation between education and the cognitive dimension of wisdom in PwS (Tables 4 and 5). Moreover, two unique patterns emerged in associations between wisdom and cognitive and mental health variables. First, wisdom and neurocognitive and functional performance were unrelated in NPCPs (0/12 analyses significant; all r^2 values ≤ 0.03), but multiple relationships emerged between wisdom and neurocognitive and functional scores in PwS (5/12 analyses significant; $r^2 = 0.05 - 0.08$). Second, whereas all three wisdom subscales were equally related to mental health, psychological traits, and quality of life in the NPCPs, the Reflective subscale showed much stronger relationships with these variables (9/9 analyses significant; mean $r^2 = 0.207$) than did the Cognitive (1/9 analyses significant; mean $r^2 = 0.016$) and Affective (0/9 analyses significant; mean $r^2 = 0.010$) subscales in PwS.

Finally, in the second exploratory analysis, PwS in the upper tertile completed more years of education (M=13.3 [2.6] years versus M=11.7 [2.2] years; t[63] = 2.44, p = .009), had a later age of onset of illness (M=29.0 [12.4] years versus M=21.9 [8.2] years; t[61] = 2.66, p = .005), fewer positive (SAPS, M=4.7 [4.4] versus 7.0 [4.1]; t[63] = 1.99, p = .025) and negative symptoms (SANS, M=4.4 [3.0] versus M=6.5 [4.0]; t[63] = 2.11, p = .020), and better functional status (UPSA-B M=76.7 [14.9] versus M=67.2 [16.4]; t[62] = 2.17, p = .017) than those in the bottom two tertiles (see Fig. 3).

4. Discussion

Wisdom appears to have a number of physical and mental health benefits (Ardelt, 2000, 2003; Roháriková et al., 2013); however, to date, the wisdom literature in psychiatric disorders is limited and there have been no investigations in PwS. To address this gap, we examined group differences in wisdom, as well as relationships between wisdom and sociodemographics, clinical symptoms, neurocognitive

Table 4Pearson's correlations between wisdom and sociodemographic, neurocognitive and functional, and mental health in PwS.

	3D-WS – cognitive	3D-WS – reflective	3D-WS – affective	3D-WS – total
Sociodemographic Age Education Gender	0.04 0.34** 0.03	-0.04 -0.13 0.04	-0.06 0.03 -0.01	-0.01 0.13 0.07
3D-WS Cognitive Reflective Affective	- 0.02 0.47**	- - 0.33**	- - -	0.71** 0.65** 0.79**
Neurocognitive and functional Processing Speed Composite Executive Functioning Composite UPSA Brief Total Score	-0.28* -0.19 0.16	-0.16 -0.08 0.22*	-0.22 -0.14 0.24 *	-0.26* -0.16 0.25*
Mental health SF-36 Mental Component Scale BSI Anxiety Scale Total Score* Calgary Depression Scale Total	0.03 0.06 -0.02	0.51** -0.52** -0.42**	0.13 -0.04 -0.04	0.36** -0.28* -0.25*
Score* Perceived Stress Scale Life Events Scale Total Score Satisfaction with Life Scale CES-D Happiness Scale* Connor Davidson Resilience	-0.03 -0.06 -0.36** 0.02 -0.06	-0.64** -0.25* 0.32** 0.36** -0.50**	-0.07 -0.14 -0.11 0.09 0.16	-0.39** -0.21 -0.05 0.25* 0.30**
10-item Scale LOT-R Optimism	-0.02	0.45**	-0.01	-23

 $PwS = people \ with \ schizophrenia$

Table 5Pearson's correlations between wisdom and sociodemographic, neurocognitive and functional, and mental health in NPCPs.

	3D-WS –	3D-WS -	3D-WS -	3D-WS -
	cognitive	reflective	affective	total
Sociodemographic				
Age	-0.20	-0.13	-0.17	-0.20
Education	0.14	-0.11	0.02	0.01
Gender (higher $=$ male)	-0.12	-0.04	-0.20	-0.15
3D-WS				
Cognitive	-	-	-	0.73**
Reflective	0.46**	-	-	0.86**
Affective	0.33**	0.56**	-	0.80**
Neurocognitive and functional				
Processing Speed Composite	-0.03	0.06	0.18	0.09
Executive Functioning Composite	-0.15	-0.08	0.13	-0.05
UPSA-B Brief Total Score	0.07	-0.03	-0.01	0.01
Mental health				
SF-36 Mental Component Scale	0.28**	0.56**	0.42**	0.54**
BSI Anxiety Scale Total Score*	-0.34**	-0.48**	-0.32^{**}	-0.48**
Calgary Depression Scale Total Score*	-0.37**	-0.44**	-0.31**	-0.47^{**}
Perceived Stress Scale	-0.42^{**}	-0.70^{**}	-0.31**	-0.61**
Life Events Scale Total Score	-0.12	-0.23*	-0.08	-0.18*
Satisfaction with Life Scale	0.22^{*}	0.61**	0.49**	0.56**
CES-D Happiness Scale*	0.34**	0.62**	0.37**	0.57**
Connor Davidson Resilience	0.44**	0.57**	0.35**	0.58**
10-item Scale	0.07**	0.07**	0.40**	0.00**
LOT-R Optimism	0.37**	0.67**	0.42**	0.62**

NPCPs = non-psychiatric control participants.

and functional performance, and mental/physical health in a wellcharacterized sample of PwS, and a sizable group of NPCPs. As predicted, PwS had lower scores than did NPCPs on the 3D-WS. Wisdom also moderated relationships between diagnostic group and neurocognitive and functional performance such that PwS with higher levels of wisdom performed better than did PwS with lower levels of wisdom. Moreover, wisdom was positively correlated with performance on multiple neurocognitive tests in PwS, but no such relationships were present in NPCPs. Consequently, it appears that wisdom and cognitive functioning overlap to a significant degree in PwS, suggesting that higher wisdom may be associated with better cognitive performance in this population. The underlying reasons for this differential relationship are not entirely clear, but may include a smaller range of values in neuropsychological performance (ceiling effects) in the NPCPs in contrast to the wellknown heterogeneity in PwS. Additionally, the reflective (but not the cognitive or affective) dimension of wisdom correlated in the expected direction with all mental health, psychological trait, and quality of life factors in PwS, suggesting that reflective wisdom may have particular clinical relevance in this population. Finally, a high-wisdom PwS group had completed more years of formal education, had a later age of onset of illness, less severe psychotic symptoms, and better overall functional status compared to a low-wisdom PwS group. One possible explanation for this effect is that wisdom confers a broad positive impact, including symptom reduction and enhanced functioning; however, the cross-sectional nature of our analyses cannot reveal the direction of the relationship.

In healthy adults, wisdom appears to reduce the negative effects of adverse life events, thereby maximizing subjective well-being (Ardelt and Jeste, 2016), life satisfaction and overall health (Ardelt, 2000), and social connectedness (Lee et al., 2019). In PwS, other related positive psychological constructs such as happiness (Palmer et al., 2014), resilience (Lee et al., 2018a, 2018b), and subjective recovery (Kukla et al., 2014) are reported to confer protection against negative mental and physical health outcomes. Our findings add to these literatures by demonstrating that PwS who are higher in wisdom perform better on

^{*} *p* < .05.

^{**} p < .01.

^{*} p < .05.

^{**} *p* < .01.

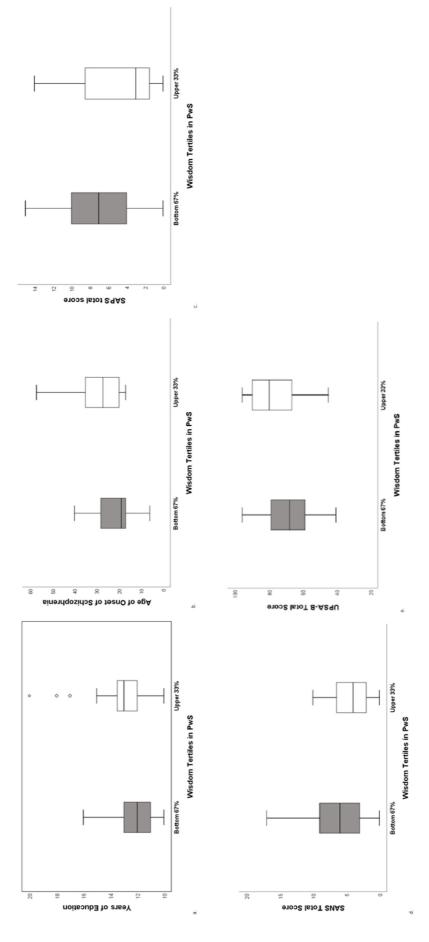


Fig. 3. Results of follow-up analyses for a) education, b) age of schizophrenia onset, c) SAPS total score, e), UPSA-B Total Score by 3D-WS tertile. Bottom two tertiles, n = 46; upper tertile, n = 19 All p's < 0.05 3D-WS = 3-Dimensional Wisdom Scale; PwS = people with schizophrenia, SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; UPSA-B = UCSD Performance-Based Assessment-Brief

neurocognitive and functional tests than do those who are lower in wisdom. Given the importance of cognition for functioning in PwS, manifesting as a) the presence of cognitive impairments decades prior to the onset of psychotic symptoms (Fischer and Aguera-Ortiz, 2018; Keefe and Harvey, 2012), as well as b) a strong link between neuropsychological measures and clinically-relevant life outcomes (Green et al., 2000, 2004), one interpretation of our data is that the subgroup of PwS with greater wisdom also have better cognitive and functional performance. Therefore, to the extent that wisdom is modifiable (Daniels et al., 2015; McLaughlin et al., 2018), it may serve as a novel target for psychological interventions aiming to reduce the negative neurocognitive effects of psychosis. However, an alternative interpretation of our results is that PwS with better social cognitive and neuropsychological functioning develop and/or retain greater wisdom. From this perspective, evidence-based interventions to improve social cognitive (Kurtz and Richardson, 2011) and neurocognitive functioning in PwS (Hogarty et al., 2004; Twamley et al., 2012) could have a positive impact on wisdom as well. Given the links between wisdom and overall wellness and quality of life (Ardelt, 2000; Ardelt, 2003; Roháriková et al., 2013; Thomas et al., 2017), the current study further supports the clinical utility of both social and neurocognitive interventions in PwS.

Social cognition is related to, but distinct from wisdom. Both are multifaceted, associated with quality of life, and aspects of both are impaired in PwS. In particular, emotion regulation (Ardelt and Jeste, 2016; Green et al., 2015) and empathy (Ardelt, 2003) underlie social cognition and wisdom. At the subscale level, reflective wisdom is related to a) social cue perception and b) mentalizing, both of which require perspective-taking. It is also possible that emotion regulation facilitates the unbiased introspection necessary for reflective wisdom. However, these social cognitive constructs do not completely capture the complexity inherent in wisdom. Additionally, on a more practical level, wisdom and social cognition differ in terms of assessment modality (i.e., self-report (Jeste and Lee, in press) versus performance-based tasks, respectively (Green et al., 2015)).

Of the three wisdom dimensions measured in the current study, only the reflective dimension of wisdom showed strong, consistent relationships with mental health, psychological traits, and quality of life in PwS. This is not surprising, given that the reflective dimension is conceptualized as the foundation for the affective and cognitive dimensions of wisdom (Ardelt, 2003). Moreover, the reflective dimension is closely tied to insight and self-awareness, which are impaired in many PwS, leading to poor clinical and functional outcomes (Lincoln et al., 2006). Indeed, Ardelt and Jeste (2016) reported that the reflective dimension was more strongly related to the well-being of healthy older adults than were other wisdom dimensions. Moreover, Khan and Ferrari (2018) administered the 3D-WS in individuals with high functioning autism (HFA) and age-matched controls and found that the HFA group scored lower on Affective and Reflective (but not Cognitive) dimensions of wisdom relative to the comparison participants. Taken together, the evidence thus far suggests that the reflective component is an important clinical marker in PwS and that interventions to increase reflective wisdom may have wide-ranging mental health benefits in this population. Although the wisdom intervention literature is still in its infancy (Jeste and Lee, in press), several studies have reported positive effects of wisdom-focused psychotherapy (Daniels et al., 2015; McLaughlin et al., 2018), further supporting future treatment efforts.

The notion that wisdom is both a trait phenomenon (Ardelt, 2003) and is amenable to intervention (Daniels et al., 2015; McLaughlin et al., 2018) may appear contradictory, as trait-based characteristics can be resistant to change (McAdams and Pals, 2006). However, similar to approaches that successfully target and ameliorate symptoms of persistent personality disorders (Shearin and Linehan, 1994; Alden, 1989), the literature on interventions to modify specific traits is promising. Other trait-based positive psychiatric characteristics such as resilience and optimism are moderately heritable (approximately 33–52%; Boardman et al., 2008), leaving a significant proportion of variance

potentially amenable to interventions. Indeed, both resilience and optimism have been improved through targeted interventions (Adler et al., 2015; Loprinzi et al., 2011). Enhancement of positive traits such wisdom thus remains possible for PwS.

The current results should be interpreted in light of several limitations. First, our sample size of PwS was moderate (n = 65), which prevented us from conducting detailed follow-up analyses on the subgroup of patients with high wisdom scores. Moreover, we analyzed a number of physical and mental health measures (nine total), which could have resulted in Type I errors. However, the pattern of results across the nine measures was consistent - PwS reported more symptoms than NPCPs in each case. Therefore, we elected to retain and report results from all of these tests, in order to provide a more comprehensive characterization of our sample. Second, the study design was crosssectional, precluding causal inference. Third, our sample was comprised of outpatients with chronic schizophrenia and, consequently, our results may not apply to inpatients or first-episode patients. Similarly, our NPCP sample was highly educated, thereby reducing generalizability to individuals with less education. Fourth, our assessment of neurocognition was limited to tests of attention/processing speed and executive functioning. Finally, wisdom has not been previously assessed in PwS and, consequently, we elected to maximize our statistical power (and correspondingly minimize the probability of Type II errors) by retaining an alpha value of 0.05. Therefore, it is possible that some of our results are false positives, although each of our primary findings was supported by at least four separate statistical tests, thereby bolstering our conclusions.

Taken together, our findings argue for the utility of measuring wisdom in PwS, as increases in wisdom may facilitate enhanced social and neurocognition, and vice versa. Furthermore, results support the notion of "wellness within illness" (Saks, 2007), whereby positive psychological characteristics are both present and measurable in people with psychiatric disorders, and higher levels of these traits promote health and well-being in subgroups of patients. In this vein, and consistent with the positive psychiatry movement (Jeste and Palmer, 2015; Lee et al., 2018a), we must resist the tendency to focus attention solely on symptoms and impairments to the exclusion of individual strengths. Instead, a sustained effort to assess and enhance positive traits such as wisdom (Roháriková et al., 2013), happiness (Palmer et al., 2014), and resilience (Lee et al., 2018a, 2018b) is likely to capitalize on the psychological assets inherent in each person with severe mental illness (see Meyer et al., 2012; Mueser et al., 2015), thereby enhancing subjective experiences and maximizing quality of life for PwS.

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Contributors

All authors made significant scientific contributions to the manuscript. Author RVP participated in conceptualizing the results, analyzed/interpreted the data, and drafted the manuscript. Author EEL assisted in conceptualization, data analysis, and writing the manuscript. Author RD assisted in study design and data collection and storage. Author XT consulted on statistical analysis and data interpretation. Author ET provided edits for the entire manuscript. Author DVJ supervised all aspects of study conceptualization, design, and implementation, as well as data analysis and interpretation. All authors approved the final version of this manuscript.

Conflicts of interest

All authors declare no conflicts of interest.

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References

Addington, D., Addington, J., Maticka-Tyndale, E., 1993. Assessing depression in schizophrenia: the Calgary Depression Scale. Br. J. Psychiatry 163, 39–44.

- Adler, A.B., Williams, J., McGurk, D., Moss, A., Bliese, P.D., 2015. Resilience training with soldiers during basic combat training: randomisation by platoon. Appl. Psychol. Health Well Being 7. 85–107.
- Alden, L., 1989. Short-term structured treatment for avoidant personality disorder. J. Consult. Clin. Psychol. 57 (6), 756–764.
- Andreasen, N.C., 1983. The Scale for the Assessment of Negative Symptoms (SANS). University of Iowa, Iowa City, Iowa.
- Andreasen, N.C., 1984. The Scale for the Assessment of Positive Symptoms (SAPS). University of Iowa, Iowa City, Iowa.
- Ardelt, M., 1997. Wisdom and life satisfaction in old age. J. Gerontol. B Psychol. Sci. Soc. Sci. 52B, P15–P27. https://doi.org/10.1093/geronb/52B.1.P15.
- Ardelt, M., 2000. Antecedents and effects of wisdom in old age: a longitudinal perspective on aging well. Res. Aging 22, 360–394. https://doi.org/10.1177/0164027500224003.
- Ardelt, M., 2003. Empirical assessment of a three-dimensional wisdom scale. Res. Aging 25, 275–324. https://doi.org/10.1177/0164027503025003004.
- Ardelt, M., Jeste, D.V., 2016. Wisdom and hard times: the ameliorating effect of wisdom on the negative association between adverse life events and well-being. J. Gerontol. B Psychol. Sci. Soc. Sci., gbw137 https://doi.org/10.1093/geronb/gbw137.
- Bangen, K.J., Meeks, T.W., Jeste, D.V., 2013. Defining and assessing wisdom: a review of the literature. Am. J. Geriatr. Psychiatry 21, 1254–1266. https://doi.org/10.1016/j. jagp.2012.11.020.
- Benedetti, F., Bernasconi, A., Bosia, M., Cavallaro, R., Dallaspezia, S., Falini, A., Poletti, S., Radaelli, D., Riccaboni, R., Scotti, G., Smeraldi, E., 2009. Functional and structural brain correlates of theory of mind and empathy deficits in schizophrenia. Schizophr. Res. 114, 154–160. https://doi.org/10.1016/j.schres.2009.06.021.
- Benton, A.L., Hamsher, K., Sivan, A.B., 1994. Multilingual Aphasia Examination (MAE). 3rd edition. Psychological Assessment Resources, Lutz.
- Boardman, J.D., Blalock, C.L., Button, T.M., 2008. Sex differences in the heritability of resilience. Twin Res. Hum. Genet. 11 (1), 12–27.
- Campbell-Sills, L., Stein, M.B., 2007. Psychometric analysis and refinement of the Connor– Davidson resilience scale (CD-RISC): validation of a 10-item measure of resilience. J. Trauma. Stress. 20 (6), 1019–1028.
- Chang, L., McBride-Chang, C., 1996. The factor structure of the life orientation test. Educ. Psychol. Meas. 56, 325–329. https://doi.org/10.1177/0013164496056002013.
- Clayton, V.P., Birren, J.E., 1980. The development of wisdom across the life span: a reexamination of an ancient topic. Life-Span Dev. Behav. 3, 103–135.
- Cohen, S., 1994. Perceived stress scale. Meas. Stress Guide Health Soc. Sci. 235-284.
- Daniels, L.R., Boehnlein, J., McCallion, P., 2015. Aging, depression, and wisdom: a pilot study of life-review intervention and PTSD treatment with two groups of Vietnam veterans. J. Gerontol. Soc. Work. 58, 420–436.
- Delis, D.C., Kaplan, E., Kramer, J.H., 2001. D-KEFS Examiners Manual. The Psychological Corporation, San Antonio, TX.
- Derogatis, L.R., Melisaratos, N., 1983. Psychol. Med. 13, 595-605.
- Diener, E., Emmons, R.A., 1985. The Satisfaction With Life Scale. p. 5.
- Etezadi, S., Pushkar, D., 2013. Why are Wise people happier? An explanatory model of wisdom and emotional well-being in older adults. J. Happiness Stud. 14, 929–950. https://doi.org/10.1007/s10902-012-9362-2.
- Farkas, M., 2007. The vision of recovery today: what it is and what it means for services. World Psychiatry 6 (2), 68–74.
- Ferrari, M., Kahn, A., Benayon, M., Nero, J., 2011. Phronesis, sophia, and hochma: developing wisdom in Islam and Judaism. Res. Hum. Dev. 8, 128–148. https://doi.org/10.1080/15427609.2011.568869.
- Fett, A.-K.J., Viechtbauer, W., Dominguez, M.-G., Penn, D.L., van Os, J., Krabbendam, L., 2011. The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. Neurosci. Biobehav. Rev. 35, 573–588. https://doi.org/10.1016/j.neubiorev.2010.07.001.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B., 2002. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition.
- Fischer, C.E., Aguera-Ortiz, L., 2018. Psychosis and dementia: risk factor, prodrome, or cause? Int. Psychogeriatr. 30, 209–219.
- González-Pablos, E., Sanguino-AndréS, R., LóPez-Villalobos, J.A., Polonia, F.I.-S., Hoyos-Villagrá, G., González-Sanguino, C., 2018. Cognitive deterioration in schizophrenia: aging and cerebrovascular disease. Int. Psychogeriatr. 1–2. https://doi.org/10.1017/S1041610218000807.
- Green, M.F., Kern, R.S., Braff, D.L., Mintz, J., 2000. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? Schizophr. Bull. 26, 119–136. https://doi.org/10.1093/oxfordjournals.schbul.a033430.
- Green, M.F., Kern, R.S., Heaton, R.K., 2004. Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. Schizophr. Res. 72, 41–51. https://doi.org/10.1016/j.schres.2004.09.009.
- Green, M., Horan, W.P., Lee, J., 2015. Social cognition in schizophrenia. Nat. Rev. Neurosci. 16, 620–631. https://doi.org/10.1038/nrn4005.
- Hayes, A., 2018. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-based Approach. 2nd ed. The Guilford Press, New York, NY.
- Hogarty, G.E., Flesher, S., Ulrich, R., Carter, M., Greenwald, D., Pogue-Geile, M., ... Parepally, H., 2004. Cognitive enhancement therapy for schizophrenia: effects of a 2-year randomized trial on cognition and behavior. Arch. Gen. Psychiatry 61 (9), 866–876.
- Hong, S., Lee, E.E., Martin, A.S., Soontornniyomkij, B., Soontornniyomkij, V., Achin, C.L., Reuter, C., Irwin, M.R., Eyler, L.T., Jeste, D.V., 2017. Abnormalities in chemokine levels in schizophrenia and their clinical correlates. Schizophr. Res. 181, 63–69.
- Horan, W.P., Hajcak, G., Wynn, J.K., Green, M.F., 2013. Impaired emotion regulation in schizophrenia: evidence from event-related potentials. Psychol. Med. 43, 2377–2391. https://doi.org/10.1017/S0033291713000019.
- Jeste, D.V., Lee, E.E., 2019. Emerging empirical science of wisdom: definition, measurement, neurobiology, longevity, and interventions. Harv. Rev. Psychiatry (in press).

- Jeste, D.V., Palmer, B.W., 2015. Positive Psychiatry: A Clinical Handbook. American Psychiatric Publishing. Washington D.C.
- Jeste, D.V., Vahia, I.V., 2008. Comparison of the conceptualization of wisdom in ancient Indian literature with modern views: focus on the Bhagavad Gita. Psychiatry Interpers. Biol. Process. 71, 197–209. https://doi.org/10.1521/psyc.2008.71.3.197.
- Jeste, D.V., Palmer, B.W., Saks, E.R., 2017. Why we need positive psychiatry for schizophrenia and other psychotic disorders. Schizophr. Bull. 43 (2), 227–229.
- Johnson, P.O., Neyman, J., 1936. Tests of certain linear hypotheses and their application to some educational problems. Stat. Res. Mem. 1, 57–93.
- Johnson, J., Gooding, P.A., Wood, A.M., Taylor, P.J., Pratt, D., Tarrier, N., 2010. Resilience to suicidal ideation in psychosis: positive self-appraisals buffer the impact of hopelessness. Behav. Res. Ther. 48, 883–889. https://doi.org/10.1016/j.brat.2010.05.013.
- Kane, J.M., Robinson, D.G., Schooler, N.R., Mueser, K.T., Penn, D.L., Rosenheck, R.A., ... Marcy, P., 2015. Comprehensive versus usual community care for first-episode psychosis: 2-year outcomes from the NIMH RAISE early treatment program. Am. I. Psychiatry 173 (4), 362–372.
- Keefe, R.S.E., Harvey, P.D., 2012. Cognitive impairment in schizophrenia. In: Geyer, M.A., Gross, G. (Eds.), Novel Antischizophrenia Treatments. Springer Berlin Heidelberg, Berlin, Heidelberg, pp. 11–37 https://doi.org/10.1007/978-3-642-25758-2_2.
- Khan, A., Ferrari, M., 2018. Wisdom of young adults with high functioning autism in Canada and Pakistan: a cross-cultural study. J. Educ. Soc. Sci. 6, 3–22. https://doi.org/10.20547/jess0611806101.
- Kukla, M., Lysaker, P.H., Roe, D., 2014. Strong subjective recovery as a protective factor against the effects of positive symptoms on quality of life outcomes in schizophrenia. Compr. Psychiatry 55, 1363–1368. https://doi.org/10.1016/j.comppsych.2014.04.022.
- Kurtz, M.M., Richardson, C.L., 2011. Social cognitive training for schizophrenia: a metaanalytic investigation of controlled research. Schizophr. Bull. 38 (5), 1092–1104.
- Lee, E.E., Eyler, L.T., Wolkowitz, O.M., Martin, A.S., Reuter, C., Kraemer, H., Jeste, D.V., 2016. Elevated plasma F2-isoprostane levels in schizophrenia. Schizophr. Res. 176, 320–326
- Lee, E.E., Lavretsky, H., Renn, B.N., Arean, P., 2018a. Positive psychiatry in geropsychiatric clinical practice: in schizophrenia, cognitive disorders, and affective disorders. Am. J. Geriatr. Psychiatry 26, 29–30.
- Lee, E.E., Martin, A.S., Tu, X., Palmer, B.W., Jeste, D.V., 2018b. Childhood adversity and schizophrenia: the protective role of resilience in mental and physical health and metabolic markers. J. Clin. Psychiatry 79. https://doi.org/10.4088/JCP.17m11776.
- Lee, E.E., Depp, C., Palmer, B.W., Glorioso, D., Liu, J., Tu, X.M., Kim, H., Tarr, P., Yamada, Y., Jeste, D.V., 2019. High Prevalence and Adverse Health Effects of Loneliness in Community-dwelling Adults Across the Lifespan: Role of Wisdom as a Protective Factor.
- Lincoln, T.M., Lullmann, E., Rief, W., 2006. Correlates and long-term consequences of poor insight in patients with schizophrenia. A systematic review. Schizophr. Bull. 33, 1324–1342. https://doi.org/10.1093/schbul/sbm002.
- Linn, B.S., Linn, M.W., Gurel, L.E.E., 1968. Cumulative illness rating scale. J. Am. Geriatr. Soc. 16, 622–626.
- Loprinzi, C.E., Prasad, K., Schroeder, D.R., Sood, A., 2011. Stress Management and Resilience Training (SMART) program to decrease stress and enhance resilience among breast cancer survivors: a pilot randomized clinical trial. Clin. Breast Cancer 11, 364–368
- Mausbach, B.T., Harvey, P.D., Goldman, S.R., Jeste, D.V., Patterson, T.L., 2006. Development of a brief scale of everyday functioning in persons with serious mental illness. Schizophr. Bull. 33, 1364–1372. https://doi.org/10.1093/schbul/sbm014.
- McAdams, D.P., Pals, J.L., 2006. A new big five: fundamental principles for an integrative science of personality. Am. Psychologist 61 (3), 204–217.
- McLaughlin, P.T., McMinn, M.R., Morse, M., Neff, M.A., Johnson, B., Summerer, D., Koskela, N., 2018. The effects of a wisdom intervention in a Christian congregation. J. Posit. Psychol. 13, 502–511. https://doi.org/10.1080/17439760.2017.1350739.
- Meyer, P.S., Johnson, D.P., Parks, A., Iwanski, C., Penn, D.L., 2012. Positive living: a pilot study of group positive psychotherapy for people with schizophrenia. J. Posit. Psychol. 7, 239–248.
- Milev, P., Ho, B.-C., Arndt, S., Andreasen, N.C., 2005. Predictive values of neurocognition and negative symptoms on functional outcome in schizophrenia: a longitudinal first-episode study with 7-year follow-up. Am. J. Psychiatry 162, 495–506. https:// doi.org/10.1176/appi.ajp.162.3.495.
- Mohamed, S., Rosenheck, R., Swartz, M., Stroup, S., Lieberman, J.A., Keefe, R.S.E., 2008. Relationship of cognition and psychopathology to functional impairment in schizophrenia. Am. J. Psychiatry 165, 978–987. https://doi.org/10.1176/appi.ajp.2008.07111713.
- Mueser, K.T., Penn, D.L., Addington, J., Brunette, M.F., Gingerich, S., Glynn, S.M., Lynde, D.W., Gottlieb, J.D., Meyer-Kalos, P., McGurk, S.R., Cather, C., Saade, S., Robinson, D.G., Schooler, N.R., Rosenheck, R.A., Kane, J.M., 2015. The NAVIGATE program for first-episode psychosis: rationale, overview, and description of psychosocial components. Psychiatr. Serv. 66, 680–690. https://doi.org/10.1176/appi.ps.201400413.
- Palmer, B.W., Martin, A.S., Depp, C.A., Glorioso, D.K., Jeste, D.V., 2014. Wellness within illness: happiness in schizophrenia. Schizophr. Res. 159, 151–156. https://doi.org/10.1016/j.schres.2014.07.027.
- Patterson, T., Goldman, S., McKibbin, C.L., Hughes, T., Jeste, D.V., 2001. UCSD performancebased skills assessment: development of a new measure of everyday functioning for severely mentally ill adults. Schizophr. Bull. 27, 12.
- Radloff, L.S., 1977. The CES-D scale: a self-report depression scale for research in the general population. Anonymous Applied Psychological Measurement. West Publishing Co., New York, NY.
- Roháriková, V., Špajdel, M., Cviková, V., Jagla, F., 2013. Tracing the Relationship Between Wisdom and Health. 55 p. 8
- Rothman, K.J., 1990. No adjustments are needed for multiple comparisons. Epidemiology 43–46.
- Saks, E.R., 2007. The Center Cannot Hold: My Journey Through Madness. Hachette, UK.

- Savla, G.N., Vella, L., Armstrong, C.C., Penn, D.L., Twamley, E.W., 2013. Deficits in domains of social cognition in schizophrenia: a meta-analysis of the empirical evidence. Schizophr. Bull. 39, 979–992.
- Schaefer, J., Giangrande, E., Weinberger, D.R., Dickinson, D., 2013. The global cognitive impairment in schizophrenia: consistent over decades and around the world. Schizophr. Res. 150. 42–50. https://doi.org/10.1016/i.schres.2013.07.009.
- Shearin, E.N., Linehan, M.M., 1994. Dialectical behavior therapy for borderline personality disorder: theoretical and empirical foundations. Acta Psychiatr. Scand. 89, 61–68.
- Sheehan, D., Lecrubier, Y., Sheehan, K., Amorim, P., Janavs, J., Weiller, E., 1998. The Mini International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and CID-10. J. Clin. Psychiatry 59, 22–33.
- Smith, M.J., Horan, W.P., Karpouzian, T.M., Abram, S.V., Cobia, D.J., Csernansky, J.G., 2012. Self-reported empathy deficits are uniquely associated with poor functioning in schizo-phrenia. Schizophr. Res. 137, 196–202. https://doi.org/10.1016/j.schres.2012.01.012.
- Spiller, S.A., Fitzsimons, G.J., Lynch, J.G., McClelland, G.H., 2013. Spotlights, floodlights, and the magic number zero: simple effects tests in moderated regression. J. Mark. Res. 50, 277–288. https://doi.org/10.1509/jmr.12.0420.
- Strauss, G.P., Kappenman, E.S., Culbreth, A.J., Catalano, L.T., Lee, B.G., Gold, J.M., 2013. Emotion regulation abnormalities in schizophrenia: cognitive change strategies fail to decrease the neural response to unpleasant stimuli. Schizophr. Bull. 39, 872–883. https://doi.org/10.1093/schbul/sbs186.
- Streiner, D.L., Norman, G.R., 2011. Correction for multiple testing: is there a resolution? Chest 140, 16–18.
- Thomas, M.L., Bangen, K.J., Palmer, B.W., Sirkin Martin, A., Avanzino, J.A., Depp, C.A., Glorioso, D., Daly, R.E., Jeste, D.V., 2017. A new scale for assessing wisdom based on

- common domains and a neurobiological model: the San Diego Wisdom Scale (SD-WISE). J. Psychiatr. Res. https://doi.org/10.1016/j.jpsychires.2017.09.005.
- Thompson, W.K., Savla, G.N., Vahia, I.V., Depp, C.A., O'Hara, R., Jeste, D.V., Palmer, B.W., 2013. Characterizing trajectories of cognitive functioning in older adults with schizophrenia: does method matter? Schizophr. Res. 143, 90–96.
- Twamley, E.W., Vella, L., Burton, C.Z., Heaton, R.K., Jeste, D.V., 2012. Compensatory cognitive training for psychosis: effects in a randomized controlled trial. J. Clin. Psychiatry 73 (9), 1212–1219.
- Ware, J.E., Sherbourne, C.D., 1992. The MOS 36-item short-form health survey (SF-36): conceptual framework and item selection. Med. Care 473–483.
- Wethington, E., 2016. Life events scale. Stress: Concepts, Cognition, Emotion, and Behavior, pp. 103–106.
- WHO Collaborating Centre for Drug Statistics Methodology, 2013. Guidelines for ATC Classification and DDD Assignment.
- WHO International Working Group for Drug Statistics Methodology, 2009. Introduction to Drug Utilization Research.
- Worthy, D.A., Gorlick, M.A., Pacheco, J.L., Schnyer, D.M., Maddox, W.T., 2011. With age comes wisdom: decision making in younger and older adults. Psychol. Sci. 22, 1375–1380. https://doi.org/10.1177/0956797611420301.
- Zacher, H., McKenna, B., Rooney, D., 2013. Effects of self-reported wisdom on happiness: not much more than emotional intelligence? J. Happiness Stud. 14, 1697–1716. https://doi.org/10.1007/s10902-012-9404-9.