Supplementary Table 1: PRISMA Checklist

Section and Topic	ltem #	Checklist item	Location where item is reported
TITLE	-		
Title	1	Identify the report as a systematic review.	Title
ABSTRACT	-		
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods and materials, search strategy
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods and materials, search strategy
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary table 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods and materials, search strategy, Supplementary Figure 1
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods and materials, data extraction and evaluation
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods and materials, data extraction and evaluation
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods and materials, data extraction and evaluation
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods and materials, data extraction and evaluation
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Methods and materials, data extraction and

Section and Topic	ltem #	Checklist item	Location where item is reported
			evaluation
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Methods and materials, data extraction and evaluation
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Methods and materials, data extraction and evaluation
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods and materials, data extraction and evaluation, Supplementary table 5-7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Methods and materials, Data synthesis and analysis
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods and materials, Data synthesis and analysis
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Methods and materials, Data synthesis and analysis
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methods and materials, data extraction and evaluation
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Methods and materials, Data synthesis and analysis
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Supplementary Figure 1 PRISMA Flowchart
-	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supplementary Figure 1 PRISMA Flowchart
Study characteristics	17	Cite each included study and present its characteristics.	Results, study selection
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Results, assessment of publication bias, quality

Results of individual studies19Results of syntheses20a20b20b20c20c	estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	assessment, Supplementary table 8 Results, supplementary figures 2-13 Tables 1-4 Tables 1-4
individual studies Results of 20a syntheses 20b	 estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing 	figures 2-13 Tables 1-4
syntheses 20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing	
200	estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing	Tables 1-4
20.0		
200	Present results of all investigations of possible causes of heterogeneity among study results.	Results, covariate assessment, assessment of publication bias supplementary figures 14-16
20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Tables 1-4
Reporting biases 21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Results, assessment of publication bias supplementary figures 14-16
Certainty of 22 evidence	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results, quality assesment
DISCUSSION		
Discussion 23a	Provide a general interpretation of the results in the context of other evidence.	Discussion
23b	Discuss any limitations of the evidence included in the review.	Discussion, limitations section
23c	Discuss any limitations of the review processes used.	Discussion, limitations section
23d	Discuss implications of the results for practice, policy, and future research.	Discussion
OTHER INFORMATION		
24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Methods and materials
24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Protocol as supplementary document
24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support 25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the	Disclosures

Section and Topic	ltem #	Checklist item	Location where item is reported
		review.	
Competing interests	26	Declare any competing interests of review authors.	Disclosures
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Collected data are not publicly available

Supplementary Table 2: Search strings on Pubmed, Web of Science and Psycinfo

platform	Search strategy
Pubmed	(schizophreni* OR schizoaffective OR psychotic OR psychosis OR MDD OR "depressive disorder" OR "major depression" OR manic OR mania OR bipolar OR "mood disorder" OR "affective disorder" OR dysthym*) AND (immun* OR chemokine* OR cytokine* OR interleukin* OR CRP OR C-reactive OR IL-1b OR IL-1β OR IL-1ra OR IL-2 OR IL-4 OR IL-6 OR IL-8 OR IL-10 OR IL-12 OR "tumor necrosis factor" OR TNF OR IFN OR IFN-γ OR Interferon* OR kynuren* OR quinolinic OR xanthurenic OR picolinic OR anthranilic OR HLA OR lymphocyt* OR monocyt* OR Leukocyt* OR neutrophil* OR basophil* or eosinophil*) AND (cogniti* OR attenti* OR vigilan* OR "executive functioning" OR reasoning OR "problem solving" OR memory OR learning OR "processing speed") NOT (review [Publication type])
Web of	(ALL=(schizophreni*) OR ALL=(schizoaffective) OR ALL=(psychotic) OR ALL=(psychosis) OR ALL=(MDD) OR ALL=(depressive disorder)
Science	OR ALL=(major depression) OR ALL=(manic) OR ALL=(mania) OR ALL=(bipolar) OR ALL=(mood disorder) OR ALL=(affective disorder) OR ALL=(dysthym*)) AND (ALL=(immun*) OR ALL=(chemokine*) OR ALL=(cytokine*) OR ALL=(interleukin*) OR ALL=(CRP) OR ALL=(C-reactive) OR ALL=(IL-1b) OR ALL=(IL-1β) OR ALL=(IL-1ra) OR ALL=(IL-2) OR ALL=(IL-4) OR ALL=(IL-6) OR ALL=(IL-8) OR ALL=(IL-10) OR ALL=(IL-12) OR ALL=(tumor necrosis factor) OR ALL=(TNF) OR ALL=(IFN) OR ALL=(IFN-γ) OR ALL=(Interferon*) OR ALL=(kynuren*) OR ALL=(quinolinic) OR ALL=(xanthurenic) OR ALL=(picolinic) OR ALL=(anthranilic) OR ALL=(HLA) OR ALL=(lymphocyt*) OR ALL=(monocyt*) OR ALL=(leukocyt*) OR ALL=(neutrophil*) OR ALL=(basophil*) OR ALL=(eosinophil*)) AND (ALL=(cognitive*) OR ALL=(attenti*) OR ALL=(vigilan*) OR ALL=(executive functioning) OR ALL=(reasoning) OR ALL=(problem solving) OR ALL=(memory) OR ALL=(learning) OR ALL=(processing speed))
Psycinfo	Any Field: schizophrenia <i>OR</i> Any Field: schizophreniform <i>OR</i> Any Field: psychotic <i>OR</i> Any Field: psychosis <i>OR</i> Any Field: MDD <i>OR</i> Any Field: depressive disorder <i>OR</i> Any Field: major depression <i>OR</i> Any Field: manic <i>OR</i> Any Field: mania <i>OR</i> Any Field: bipolar <i>OR</i> Any Field: mood disorder <i>OR</i> Any Field: affective disorder <i>OR</i> Any Field: dysthymia <i>AND</i> Any Field: Immune OR cytokine OR chemokine OR interleukin OR CRP OR IL-1b OR IL-1β OR IL-1ra OR IL-2 OR IL-4 OR IL-6 OR IL-8 OR IL-10 OR IL-12 OR tumor necrosis factor OR TNF OR IFN OR IFN-γ OR Interferon OR kynurenine OR kynurenic OR quinolinic OR xanthurenic OR picolinic OR anthranilic OR HLA OR lymphocyte OR monocyte OR Leukocyte OR neutrophil OR basophil or eosinophil <i>AND</i> Any Field: cognition <i>OR</i> Any Field: cognitive <i>OR</i> Any Field: attention <i>OR</i> Any Field: vigilance <i>OR</i> Any Field: memory <i>OR</i> Any Field: learning <i>OR</i> Any Field: processing speed <i>AND</i> Peer-Reviewed Journals only

Supplementary Table 3: Investigated cognitive domains and cognitive tests included

Domain	Tests
Verbal learning and memory	List learning tasks (RBANS-memory, BACS, CVLT, RaVLT,)
Visual learning and memory	RBANS-visuospatial; pairs matching test;
Working memory	LNS, Letter sequencing, Digit backward, spatial span test, Digit sequencing test, BACS- WM, MCCB-WM, delayed match to sample test,
Attention and vigilance	RBANS-attention, MCCB-attention, BACS-attention, CANTAB-attention, CPT, Digit span, simple reaction time
Processing speed	Digit Symbol Coding tests, TMTB
Reasoning and problem solving	WCST, Tower of London, CANTAB-set shift, Stroop test, Mazes, BACS-EF, abstraction test, matrix reasoning, MCCB reasoning,
Language	RBANS-language, Verbal Fluency tests, COWAT, naming test

Supplementary Table 4: Included inflammatory markers

Category	Inflammatory markers
Pro-inflammatory markers	(hs)CRP, IL-1b, IL-2, IL-3, IL-6, IL-7, IL-8, IL-12-p70, IL-15, IL-16, IL-17, IL-18, IL-33, IFN-
	g, TNF-a, TNF-b, sTNFR1, sTNFR2, CCL-11, CCL-17, CCL-22, CXCL-10, MCP-1, sST2
Anti-inflammatory markers	IL-1ra, IL-4, IL-10, IL-11, IL-13, TGFb

Study Name	year	Diagnosis	Ν	mean age	DOI	BMI	%mP	smoking%
Ali	2018	MDD	40	64,1	29,4	24,01	53	NR
Amin	2020	SZ	50	35,4	NR	21,6	76	NR
Asevedo	2013	SZ	30	33,7	NR	NR	83	48
Asevedo	2014	SZ	29	33,2	11,8	NR	83	46
Barbosa	2018	BD	20	43,8	20,2	NR	25	NR
Barbosa	2012	BD	25	50,9	27,9	29,1	32	NR
Belge	2021	MDD	62	58,2	NR	24,6	23	21
Bobinska	2016	MDD	89	39,9	7	NR	44	NR
Boozalis	2018	SZ	39	32,8	NR	27,3	74	NR
Borovcanin	2020	SZ	27	36,2	9,95	25,4	59	NR
Cathomas	2021	MDD	44	35,8	7	22,9	40	23
		SZ	45	34	10,1	26,4	69	64
Chakrabarty	2018	BD	51	23,2	25,3	25,2	47	NR
Chang	2012	MDD	112	38,8	NR	NR	28	16
Chung	2013	BD	17	31,3	8,3	23,3	23,3	41
Dal Santo	2020	SZ	132	37,8	8,93	28,2	62	49
de Campos-Carli	2017	SZ	40	40,8	11,9	NR	53	NR
De Picker	2020	SZ	49	32,4	6,1	24,9	86	64
Doganavsargil-Baysal	2013	BD	54	39,5	12,5	NR	33	NR
Dorofeikova	2018	SZ	125	35,8	12	NR	58	NR
Elderkin-Thompson	2012	MDD	42	69,7	NR	25,6	33	NR
Ergun	2018	SZ	30	36,4	11,4	27,2	70	53
Fang	2019	SZ	174	35,8	NR	24,1	47	NR
Fathian	2019	SZ	208	33,5	NR	23,7	69	NR

Supplementary Table 5: Demographic characteristics of included studies

	1	1	-					
Frydecka	2015a	SZ	151	37,8	12,2	NR	46	NR
Frydecka	2015b	SZ	151	37,8	12,2	NR	46	NR
Goldsmith	2016	MDD	93	39,4	NR	31,5	NR	NR
Grassi-Oliveira	2011	MDD	30	39,2	11,5	25,8	NR	NR
Hori	2016	SZ	146	33,6	8,7	NR	51	36
Huang	2020	SZ	30	27,6	2,9	NR	50	NR
Jin	2020	MDD	100	27,8	NR	NR	38	NR
Johnsen	2016	SZ	124	33 <i>,</i> 5	NR	23,5	68	52
Joseph	2015	SZ	88	49,4	23,6	31	39,4	49
Kindler	2020	SZ	96	35,7	12,9	NR	61	49
King	2021	SZ	104	42	NR	29,5	70	NR
Klaus	2021	SZ	16	42	NR	NR	25	NR
Kogan	2018	SZ	32	37	NR	31,1	64	24
Kudo	2018	SZ	87	42,5	12,3	NR	50	NR
Lizano	2019	SZ	223	35,1	15,5	NR	66	NR
		BD	190	36,1	19,5	NR	31	NR
Lizano	2021	SZ	140	34,3	18,5	NR	43	NR
Malmqvist	2019	SZ	41	28	0,5	21,6	63	8
Martinez- Cengotitabengoa	2012	SZ	28	27,7	0	NR	75	NR
Miller	2012	SZ	31	31	10,4	25,8	61	45
Millet	2020	BD	222	44	NR	29,9	53	NR
Millet	2015	BD	219	44	22	29,9	53	NR
Milton	2020	BD	969	55,5	NR	28,2	54	NR
	2021	MDD	22441	56	NR	27,8	51	NR
Mora	2018	BD	84	45,1	NR	27,8	52	NR
Moustafa	2018	SZ	115	36,3	8	28,9	68	NR
ivioustala	2020	52	112	50,5	0	20,9	00	INIT

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North	2021	SZ	499	39,6	15,8	NR	65	72
Noyan	2021	SZ	150	31,6	5,6	25,2	75	56
Orhan	2018	SZ	25	28,5	NR	21,8	71	26
Peters	2019	MDD	40	14,5	2,4	NR	40	NR
Qu	2019	MDD	104	34,1	9,3	22,7	36	19
Rahmani	2021	BD	26	17,6	1,9	21,9	42	15
Reboucas	2018	SZ	35	40	NR	26,1	69	43
Ribeiro-Santos	2019	SZ	63	42,4	15,9	25,6	52,4	30,1
Sanchez-autet	2018	BD	224	47,1	19,5	28,5	34,7	45,2
Saraykar	2018	MDD	74	73	NR	26,6	9	NR
Smagula	2017	MDD	31	68,8	NR	30,9	77	NR
Strawbridge	2021	BD	44	43,7	NR	27,8	30	NR
Tanaka	2017	BD	32	39	NR	NR	64	39
Tateishi	2020	MDD	11	52,2	6	NR	55	NR
Tseng	2019	BD	24	36,5	NR	NR	36	24
Van den Ameele	2020	BD	67	43,1	NR	25,3	48	36
Vinberg	2016	MDD	44	43	NR	26	69	NR
Weiser	2019	SZ	200	43	13	NR	44	NR
Wilson	2018	SZ	14	47	NR	40	0	57
Wu	2016	SZ	70	46,2	21,5	24,9	41	68
Xiu	2016	SZ	128	26,4	1	20,1	59	28
Xiu	2018	SZ	45	26,4	1	20,1	59	28
Ye	2018	MDD	30	42,6	5,8	22,9	40	17
Zazula	2021	BD	31	40	19	28	19	NR
Zhang	2013	SZ	77	29,2	2,7	22,6	52	25
Zhang	2021	SZ	75	NR	NR	NR	NR	NR
Zhou	2021	MDD	149	39	NR	22	22	15

Study Name	year	Diagnosis	# markers	Inflammation marker
Ali	2018	MDD	1	IL-6
Amin	2020	SZ	1	TNF-a
Asevedo	2013	SZ	6	CXCL-10/IP-10, CXCL-8/IL-8, CCL-11, CCL-24/Eotaxin-2, CCL-2/MCP-1, CCL-3/MIP-1
Asevedo	2014	SZ	1	IL-2
Barbosa	2018	BD	9	IL2, IL4,IL6,IL10,IFNg,TNFa,IL17a,sTNFR1,sTNFR2
Barbosa	2012	BD	3	TNF-a, TNFR1, sTNFR2
Belge	2021	MDD	7	IL6,IL1b,IFNg,CRP,IL8,TNFa, IL-10
Bobinska	2016	MDD	3	TNFa, TNFRSF1A, TNFRS1B
Boozalis	2018	SZ	1	CRP
Borovcanin	2020	SZ	4	IL-17, IL-6, TNF-a; sST2)
Cathomas	2021	MDD, SZ	5	TRYCATS
Chakrabarty	2018	BD	5	IL1b,IL4,IL6,IL10,TNFa
Chang	2012	MDD	1	CRP
Chung	2013	BD	1	hs-CRP
Dal Santo	2020	SZ	1	CRP
de Campos-Carli	2017	SZ	2	IL-33, sST2
De Picker	2020	SZ	12	TRYCATS, CRP, IL6
Doganavsargil- Baysal	2013	BD	3	TNFa, sTNFR1, sTNFR2
Dorofeikova	2018	SZ	1	CRP
Elderkin- Thompson	2012	MDD	2	CRP, IL-6
Ergun	2018	SZ	2	IL-6, TNFa
Fang	2019	SZ	1	IL-6
Fathian	2019	SZ	1	CRP

Supplementary Table 6: included immunomarkers in the included studies

Frydecka	2015a	SZ	2	hs-CRP, IL-6
Frydecka	2015b	SZ	1	TGF-b
Goldsmith	2016	MDD	8	TNF, IL1b, IL6,IL10, MCP1,IL1RA,IL6sr, TNFr2
Grassi-Oliveira	2011	MDD	2	IL-6, TNFa
Hori	2016	SZ	2	IL-6, TNF-a
Huang	2020	SZ	3	TRP, KYN, KYNA
Jin	2020	MDD	2	IL-1b, IL-6
Johnsen	2016	SZ	1	CRP
Joseph	2015	SZ	1	hs-CRP
Kindler	2020	SZ	10	TRP, KYN, KYNA, 3HK, QUINA, CRP, IL-1, IL6, IL-8, IL-18
King	2021	SZ	1	IL6
Klaus	2021	SZ	13	CRP, IL6, IL-10, IP-10, IFNg, TNFa, Eotaxin, MCP1, MIP1b, Fractalkine, SAA, ICAM1, VCAM1
Kogan	2018	SZ	4	IL-1b, IL-6, TNFa, IL-12p70
Kudo	2018	SZ	1	sTNFR2
Lizano	2019	SZ, BD	12	CRP, IL6, TNFa, IL1a, IL1b, IL4, IL8, IL10, IL12, IL23, IL12p70, IFNg
Lizano	2021	SZ	12	CRP, IL6, TNFa, IL1a, IL1b, IL4, IL8, IL10, IL12, IL23, IL12p70, IFNg
Malmqvist	2019	SZ	4	TARC/CCL17, eotaxin/CCL11, MDC/CCL22, IP-10/CXCL10
Martinez- Cengotitabengoa	2012	SZ	1	MCP-1
Miller	2020	SZ	13	IL-6, CRP, IL17, IL1a, IL1b, IL1RA, IL4,IL6,IL8,IL10,MCP1,sCD40L,TNFa
Millet	2019	BD	1	CRP
Millet	2020	BD	3	TNFa sTNF-R1, sTNF-R2
Milton	2021	BD	1	CRP
Milton	2021	MDD	1	CRP
Mora	2018	BD	3	TNF-a, IL10, IL6
Moustafa	2020	SZ	3	IL6, IL10, CRP
North	2021	SZ	1	CRP

Noyan	2021	SZ	4	TRP, KYN, KYNA, IL-1b
Orhan	2018	SZ	1	IL-18
Peters	2019	MDD	3	IL6,IL1b, TNFa
Qu	2019	MDD	3	CRP, IL1b, IL6
Rahmani	2021	BD	6	CRP,IL1b, IL6, IL10, IL4, TNFa
Reboucas	2018	SZ	2	TNF-a, IL-6
Ribeiro-Santos	2019	SZ	7	IL2, IL4, IL6, IL10,IL17a,TNFa,IFNg
Sanchez-autet	2018	BD	1	CRP
Saraykar	2018	MDD	1	IL17A
Smagula	2017	MDD	7	TNFa, IL2, IL4, IL6, IL10, IL17, MCP-1
Strawbridge	2021	BD	19	CRP, IFNg, IL10, IL12, IL15,IL16,IL17,IL1a,IL6,IL7,IL8,IP10,MCP1,MCP4,MIP1a,MIP1b,TARC,SAA,TNFa,TNFb
Tanaka	2017	BD	1	CRP
Tateishi	2020	MDD	3	IL1b, IL6, TNFa
Tseng	2019	BD	1	CRP
Van den Ameele	2020	BD	10	CRP, TNF-α, IFN-y, IL-1β, IL-4, IL-6, TRP, KYN, KYNA, QA
Vinberg	2016	MDD	3	hsCRP, IL18, IL6
Weiser	2019	SZ	1	CRP
Wilson	2018	SZ	1	IFNg
Wu	2016	SZ	1	I-18
Xiu	2016	SZ	1	IL-10
Xiu	2018	SZ	1	IL-3
Ye	2018	MDD	1	IL6
Zazula	2021	BD	3	TNF-a, sTNFR1, sTNFR2
Zhang	2013	SZ	3	IL-1b, IL-6, TNFa
Zhang	2021	SZ	2	IL-1b, TNFa
Zhou	2021	MDD	3	TRP, KYN, KA

Study Name	year	Diagnosis	VeM&L	ViM&L	wм	A&V	PS	La	R/P	sc	GC
Ali	2018	MDD	x			x	x	x			x
Amin	2020	SZ									x
Asevedo	2013	SZ	x		x		x	x	x		x
Asevedo	2014	SZ	x		x		x	x	x		x
Barbosa	2018	BD	x		x		x	x		x	x
Barbosa	2012	BD							x		
Belge	2021	MDD	x				x				
Bobinska	2016	MDD	x				x	x			x
Boozalis	2018	SZ	x	x	x	x	x	x			x
Borovcanin	2020	SZ									x
Cathomas	2021	MDD			x		x				x
Cathomas	2021	SZ			x		x				x
Chakrabarty	2018	BD	x	x	x	x	x	x		х	x
Chang	2012	MDD				x			x		x
Chung	2013	BD							x		
Dal Santo	2020	SZ	x	x	x	x	x	x	x	x	x
de Campos-Carli	2017	SZ									x
De Picker	2020	SZ			x		x				
Doganavsargil- Baysal	2013	BD	x						x		
Dorofeikova	2018	SZ	x		x		x		x		x
Elderkin-Thompson	2012	MDD	x	x		x	x		x		x
Ergun	2018	SZ	x	x	x	x	x	x	x		x
Fang	2019	SZ	x	x		x		x			x
Fathian	2019	SZ	x	x		x		x			x
Frydecka	2015a	SZ	x		x	x	x		x		x

Supplementary Table 7: Overview of the cognitive domains assessed per included study

Frydecka	2015b	SZ	x		x	x	x		x		х
Goldsmith	2016	MDD					x				
Grassi-Oliveira	2011	MDD	х								
Hori	2016	SZ	x		x	х	x		х		x
Huang	2020	SZ	x	x	x	x	x		x	x	x
Jin	2020	MDD	x	x	x	x	x		x	x	x
Johnsen	2016	SZ	x	x		x		x			x
Joseph	2015	SZ									
Kindler	2020	SZ	x		x	x	x				x
King	2021	SZ					x	x	x	x	x
Klaus	2021	SZ					x				
Kogan	2018	SZ	x	x	x	x	x		x	x	x
Kudo	2018	SZ	x	x							x
Lizano	2019	SZ	x		x	x	x	x	x	x	x
Lizano	2019	BD	x		x	x	x	x	x	x	x
Lizano	2021	SZ	x		x	x	x	x	x	x	x
Malmqvist	2019	SZ	x	x	x	x	x		x	x	x
Martinez- Cengotitabengoa	2012	SZ									
			x		x	x	x		x		x
Miller	2020	SZ	x								
Millet	2019	BD	x	x	x	x	x		x	x	x
Millet	2020	BD	х	x	x	x	x		х	x	х
Milton	2021	BD		x			х				x
Milton	2021	MDD		x			x				x
Mora	2018	BD	x	x		x	x	x			x
Moustafa	2020	SZ	x		x		x	x	x		x
North	2021	SZ	x	x		x		x			x
Noyan	2021	SZ					x		x		x
Orhan	2018	SZ	x	x	x	x	x		x	x	x

1			1	1			1		r - r	
Peters	2019	MDD				x	x			
Qu	2019	MDD								x
Rahmani	2021	BD						x	x	x
Reboucas	2018	SZ	x							
Ribeiro-Santos	2019	SZ	x		x		x		x	x
Sanchez-autet	2018	BD	x		x		x	x		
Saraykar	2018	MDD	x	x		x			x	x
Smagula	2017	MDD					x			
Strawbridge	2021	BD	x		x		x		x	
Tanaka	2017	BD								x
Tateishi	2020	MDD					x	x	x	x
Tseng	2019	BD				x			x	x
Van den Ameele	2020	BD			x		x			x
Vinberg	2016	MDD	x							
Weiser	2019	SZ	x	x	x		x		x	x
Wilson	2018	SZ	x	x		x		x		x
Wu	2016	SZ	x	x		x		x		x
Xiu	2016	SZ	x	x		x		x		x
Xiu	2018	SZ	x	x		x		x		x
Ye	2018	MDD		x		x		x		
Zazula	2021	BD	x	x	x	x	x		x	x
Zhang	2013	SZ	x	x	x	x	x		x	 x
Zhang	2021	SZ	x	x	x	x	x		x	 x
Zhou	2021	MDD	x	x	x		x			 x

Legend: VeM&L: Verbal Memory and Learning; ViM&L: Visual Memory and Learning; WM: Working Memory; A&V: Attention and Vigilance; PS:

Processing Speed; La: Language; R/P: Reasoning/Problem Solving; SC: Social Cognition; GC: Global Cognition

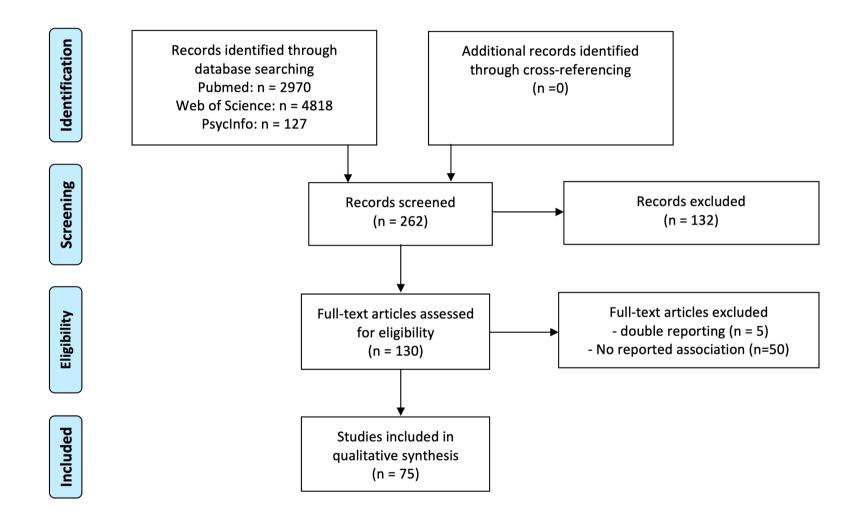
Study Name	year	1.	2. Study	3. St	4. Study	5. Stat.	6. Context-	7.	8.	9.	10. Biomarker	SUM	Quality
		Нуро	pop. sel	рор	рор	analysis	specific disc.	Study	assay	Labo	data modeling		
		thesis		rep	char			limit.	methods	meas.			
Ali	2018	1	1	1	0	0	1	1	0	0	0	5	Moderate
Amin	2020	1	1	1	0	0	1	1	0	0	0	5	Moderate
Asevedo	2013	1	1	0	1	1	1	1	1	0	1	8	High
Asevedo	2014	1	1	0	1	1	1	1	0	0	0	6	Moderate
Barbosa	2018	1	1	0	0	1	1	1	1	0	0	6	Moderate
Barbosa	2012	1	1	0	1	0	1	0	1	0	1	6	Moderate
Belge	2021	1	1	0	0	0	1	0	1	0	0	4	Moderate
Bobinska	2016	1	1	0	0	0	1	0	1	0	0	4	Moderate
Boozalis	2018	1	1	0	1	1	1	1	0	0	0	6	Moderate
Borovcanin	2020	1	1	0	1	0	1	1	0	0	0	5	Moderate
Cathomas	2021	1	1	0	1	1	1	0	1	0	0	6	Moderate
Chakrabarty	2018	1	1	0	0	1	1	1	0	0	1	6	Moderate
Chang	2012	1	1	1	1	1	1	1	1	0	1	9	High
Chung	2013	1	1	0	1	1	1	0	1	0	0	6	Moderate
Dal Santo	2020	1	1	1	1	1	1	1	0	0	0	7	High
de Campos-Carli	2017	1	1	0	1	1	1	0	1	0	0	6	Moderate
De Picker	2020	1	1	0	1	1	1	1	1	0	1	8	High
Doganavsargil-Baysal	2013	1	1	1	1	1	1	1	0	0	1	8	High
Dorofeikova	2018	1	1	0	0	0	1	1	0	0	0	4	Moderate
Elderkin-Thompson	2012	1	1	0	1	1	1	1	1	0	0	7	High
Ergun	2018	1	1	0	1	1	1	1	0	0	1	7	High
Fang	2019	1	1	1	1	1	1	1	1	0	1	9	High
Fathian	2019	1	1	0	1	1	1	1	1	0	0	7	High

Supplementary Table 8: BIOCROSS quality assessment of the included studies

Frydecka	2015b	1	1	0	1	1	1	1	1	0	0	7	High
Frydecka	2015a	1	1	0	0	1	1	0	1	1	0	6	Moderate
Goldsmith	2016	1	1	0	0	1	1	0	1	0	0	5	Moderate
Grassi-Oliveira	2011	1	1	0	1	1	1	1	1	0	0	7	High
Hori	2016	1	1	1	0	1	1	1	1	0	0	7	High
Huang	2020	1	1	0	0	1	1	0	0	0	0	4	Moderate
Jin	2020	1	1	0	1	1	1	0	1	0	1	7	High
Johnsen	2016	1	1	0	1	1	1	0	1	0	0	6	Moderate
Joseph	2015	1	1	0	1	1	1	1	0	0	0	6	Moderate
Kindler	2020	1	1	0	0	0	1	1	1	0	1	6	Moderate
King	2021	1	1	0	1	1	1	1	1	0	0	7	High
Klaus	2021	1	1	0	0	1	1	1	0	0	0	5	Moderate
Kogan	2018	1	1	0	1	0	1	0	1	0	0	5	Moderate
Kudo	2018	1	1	0	1	1	1	0	1	1	1	8	High
Lizano	2019	1	1	0	1	1	1	1	1	0	0	7	High
Lizano	2021	1	1	0	1	1	1	1	1	1	1	9	High
Malmqvist	2019	1	1	0	1	1	1	0	1	1	0	7	High
Martinez- Cengotitabengoa	2012	1	1	0	0	1	1	0	1	0	0	5	Moderate
Miller	2020	1	1	1	1	1	1	0	1	0	0	7	High
Millet	2019	1	1	1	1	1	1	1	1	1	0	9	High
Millet	2020	1	1	0	1	1	1	0	1	0	0	6	Moderate
Milton	2021	1	1	1	1	1	1	0	1	0	0	7	High
Mora	2018	1	1	0	1	1	1	1	1	0	1	8	High
Moustafa	2020	1	1	1	1	1	1	0	1	0	1	8	High
North	2021	1	1	0	1	1	1	1	1	0	0	7	High
Noyan	2021	1	1	0	1	1	1	1	1	0	0	7	High
Orhan	2018	1	1	0	0	1	1	0	0	0	0	4	Low

Peters	2019	1	1	0	1	1	1	1	1	0	1	8	High
Qu	2019	1	1	0	1	1	1	1	1	0	0	7	High
Rahmani	2021	1	1	1	1	1	1	1	0	0	1	8	High
Reboucas	2018	1	1	0	1	1	1	0	1	0	0	6	Moderate
Ribeiro-Santos	2019	1	1	0	0	1	1	1	1	1	0	7	High
Sanchez-autet	2018	1	1	0	1	1	1	0	0	0	0	5	Moderate
Saraykar	2018	1	1	0	0	1	1	1	1	0	0	6	Moderate
Samagula	2017	1	1	0	1	1	1	1	1	0	1	8	High
Strawbridge	2021	1	1	0	1	1	1	1	1	0	1	8	High
Tanaka	2017	1	1	0	1	1	1	1	0	0	0	6	Moderate
Tateishi	2020	1	1	0	0	0	1	0	1	1	0	5	Moderate
Tseng	2019	1	1	0	1	1	1	1	0	0	0	6	Moderate
Van den Ameele	2020	1	1	0	0	1	1	1	1	0	1	7	High
Vinberg	2016	1	1	0	0	0	1	0	1	1	0	5	Moderate
Weiser	2019	1	1	1	0	1	1	1	1	0	0	7	High
Wilson	2018	1	1	1	1	1	1	0	0	0	0	6	Moderate
Wu	2016	1	1	0	1	1	1	1	1	1	0	8	High
Xiu	2016	1	1	0	1	1	1	1	1	0	0	7	High
Xiu	2018	1	1	0	1	1	1	0	0	1	0	6	Moderate
Ye	2018	1	1	0	0	0	1	1	1	1	1	7	High
Zazula	2021	1	1	0	1	1	1	0	0	0	0	5	Moderate
Zhang	2013	1	1	0	1	1	1	0	1	1	0	7	High
Zhang	2021	1	1	0	0	1	1	0	0	0	0	4	Low
Zhou	2021	1	1	0	1	1	1	0	1	0	0	6	Moderate

Supplementary Figure 1: PRISMA Flowchart



Supplementary Figure 2: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and Global Cognition for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

1.00

Dome Lower Upper Zubus p-Value BD Lizaro 2019 BD -0.006 -0.007 -3.98 0.167 BD Doganzwargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargil-Bayargi	Group by Subgroup within study	<u>Study nam</u> e	Diagnosis	s St	tatistics	for eac	<u>h stud</u> y				Correlation and 95% CI
BD Miton 2021 BD -0.027 0.089 0.037 0.824 0.410 0.439 BD Degravarsgil-Bayes/2018D -0.001 0.356 0.156 0.714 0.419 BD Brockes 2018 BD -0.001 0.356 0.348 0.055 0.986 BD Brockes 2018 BD -0.027 0.387 0.023 2.086 0.030 BD Moma 2016 BD -0.027 0.387 0.023 2.086 0.030 BD Moma 2016 BD -0.017 0.144 0.115 0.224 0.801 BD Milei 2019 BD -0.017 0.144 0.155 0.284 0.802 BD Van den Ameele 2020 BD -0.024 0.386 0.244 0.081 0.702 BD Zanula 2021 BD -0.026 0.266 0.260 0.266 0.265 0.161 0.702 BD Calueria 2019 MDD -0.168 0.226 0.266 0.266 0.266 0.266 0.266 0.266 0.266 0.266	Subgroup within study			Correlation			Z-Value	p-Value			
BD Doganavargil-Bayal 20BD -0.10 0.36 0.174 0.439 BD Barloss 2016 BD -0.64 -0.75 -0.62 -0.26 -0.44 BD Charmberty 2018 BD -0.64 -0.75 -0.63 -2.066 0.440 BD Charmberty 2018 BD -0.27 -0.387 -0.144 -1.16 0.000 BD Samchaz-aulut 2016 BD -0.27 0.387 -0.144 -1.16 0.000 BD Mill 2.17 0.387 0.144 0.116 0.122 0.820 BD Van den Ameel 2020 BD -0.217 0.387 0.144 0.116 0.220 0.820 BD Van den Ameel 2020 BD -0.618 -0.227 0.230 0.241 0.355 0.111 MDD Charg 2012 MDD -0.280 0.250 0.256 0.556 0.111 MDD Bole 32.21 MDD 0.250 0.456 0.086 -2516 0.112 MDD Bole 32.21 MDD 0.116 0.256	BD			-0.096	-0.235	0.047	-1.318	0.187		- I	
BD Tankas 2017 BD 0.001 0.350 0.348 0.005 0.098 BD Barbonsa 2018 BD 0.333 0.557 0.003 2.309 0.0140 BD Mana 2018 BD 0.333 0.557 0.063 2.339 0.049 BD Similar 2018 BD 0.000 0.214 0.214 0.216 0.090 BD Similar 2018 BD 0.007 0.234 0.114 0.12 0.807 BD Van den Ameele 2020 BD 0.026 0.287 0.213 0.228 0.820 BD Zazula 2021 BD 0.070 0.291 0.414 0.373 0.708 BD Zazula 2021 BD 0.070 0.291 0.414 0.373 0.708 BD Zazula 2021 BD 0.077 0.291 0.414 0.373 0.708 BD Zazula 2021 MDD 0.106 0.202 0.214 0.436 0.560 0.564 0.561 0.564 0.577 0.500 MDD Caldemin 2	BD										
BD Barbosa 2018 BD -0.461 0.750 -0.023 -0.256 0.040 BD Mora 2018 BD 0.000 -0.214 0.215 0.002 0.989 0.116 BD Mora 2018 BD 0.000 -0.214 0.217 0.307 0.116 0.000 BD Mark 2018 BD -0.207 0.214 0.217 0.228 0.820 BD Vian dan Ameeia 2020 BD -0.269 0.218 0.228 0.820 BD Zaruda 2021 BD 0.068 0.243 0.349 0.373 0.709 BD Zaruda 2021 BD 0.068 0.216 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.288 0.168 0.228 0.379 0.070 0.281 0.388 0.388 0.388 0.388 0.388 0.388 0.388 0.388											-
BD Chakmbardy 2018 BD 0.000 0.557 0.003 2.399 0.001 0.000 BD Sanchez-aulet 2018 BD 0.207 0.387 0.144 0.114 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.144 0.143 0.240 0.240 0.240 0.240 0.240 0.240 0.240 0.240 0.240 0.240 0.241 0.250 0.240 0.241 0.250 0.247 0.213 0.247 0.213 0.247 0.210 0.246 0.247 0.210 0.250 0.211 0.025 0.214 0.255 0.251 0.036 0.111 0.046 0.230 0.251 0.012 0.444 0.373 0.051 0.454 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.246 0.256 0.2466 0.056											
BD Mora 2018 BD 0.000 0.214 0.215 0.009 0.9999 BD Sanchez-autel 2018 BD -0.017 -0.148 0.115 0.244 0.112 0.269 BD Milet 2019 BD -0.017 -0.148 0.116 -0.241 0.267 0.268 -0.020 0.268 -0.020 0.268 -0.020 0.268 -0.020 -0.020 0.268 -0.020 -0.020 -0.020 -0.020 -0.020 -0.020 -0.020 -0.020 -0.020 -0.021 -0.020 -0.021 -0.020 -0.021 -0.020 -0.020 -0.021 -0.020 -0.021 -0.020 -0.021 -0.020 -0.020 -0.021 -0.020 -0.020 -0.021 -0.020 -0.021 -0.020 -0.021 -0.020 -0.021 -0.020 -0.021 -0.020 -0.021 -0.020 -0.211 -0.020 -0.026 -0.021 -0.020 -0.021 -0.020 -0.021 -0.020 -0.028 -0.028 -0.028 -0.021 -0.020 -0.021 -0.020 -0.021 -0.010											
BD Samchez-autel 2018 BD -0.270 -0.387 -0.144 -0.148 -0.16 -0.244 0.800 BD Tiseng 2019 BD -0.241 0.587 0.218 -0.228 0.820 BD Strawbridge 2021 BD -0.241 0.587 0.218 0.224 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.228 0.218 0.018 0.025 BD Zaxula 2021 BD -0.095 0.016 0.022 2.236 0.018 0.025 MDD Chang 2012 MDD -0.056 0.028 -0.286 0.281 0.396 0.011 0.025 0.014 0.016 0.225 0.014 0.016 0.225 0.014 0.016 0.226 0.014 0.256 0.016 0.256 0.014 0.256 0.014 0.256 0.014 0.256 0.014 0.256 0.014 0.256 0.014 0.256 0.027 0.251 0.456 0.026 0.256 0.046 0.026 0.266 0.26											
BD Milet 2019 BD -0.017 -0.148 0.115 -0.244 0.807 BD Tanga 2019 BD -0.024 0.287 0.180 -1.127 0.280 BD Van den Ameele 2020 BD 0.029 0.287 0.180 -7.127 0.280 BD Zarula 2021 BD 0.029 0.281 0.241 0.374 0.709 BD Carula 2012 BD 0.016 0.026 -0.584 -1.484 0.010 MDD Eidenkin-Thompson 2012 MDD -0.254 0.244 0.365 0.156 0.956 0.956 0.911 MDD Goldsmith 2016 MDD -0.156 0.477 0.203 0.214 0.012 -0.255 0.456 0.456 0.911 MDD Goldsmith 2016 MDD -0.139 -0.180 -0.244 0.206 -1.480 0.208 -1.244 0.208 -1.244 0.208 -1.244 0.2012 -1.246 0.2015 -2.440 0.000 -2.440 0.206 -2.440 0.207 0.208 -2.440 0.208											
BD Tseng 2019 BD -0.241 -0.587 0.180 -1.127 0.260 BD Van den Ameel 2020 BD 0.056 0.247 0.213 0.028 0.826 BD Strawtridge 2021 BD 0.056 0.243 0.349 0.374 0.706 BD Carula 2021 DD 0.070 0.281 0.414 0.373 0.706 BD Carula 2021 DD 0.021 0.241 0.314 0.035 0.035 BD Carula 2021 DD 0.216 0.160 0.056 2.236 0.025 0.035 MDD Eiderkin-Thompson 2012 MDD -0.250 0.231 0.414 0.956 0.958 MDD BD 0.138 0.056 0.466 0.660 0.548 0.990 MDD Ya 2018 MDD 0.115 0.256 0.337 0.290 0.346 0.360 0.346 0.271 0.360 MDD Qu 2019 MDD 0.046 0.272 0.277 0.066 0.548 0.000 0.038 0.733											
BD Van den Ameele 2020 BD -0.029 -0.267 0.213 -0.208 0.820 BD Zazula 2021 BD 0.005 0.243 0.344 0.709 BD -0.005 0.168 0.025 -2.474 0.013 MDD Chang 2012 MDD -0.211 -0.382 0.025 0.244 0.041 0.025 MDD Bolinska 2016 MDD -0.211 -0.382 0.026 -2.474 0.001 MDD Bolinska 2016 MDD -0.210 0.377 0.269 0.184 0.225 MDD All 2018 MDD -0.152 0.267 0.268 0.060 0.061 MDD All 2018 MDD -0.139 0.480 0.805 0.001 0.002 MDD MDD 0.464 0.603 0.288 0.604 0.205 0.006 MDD MDD 0.059 0.454 0.050 0.285 0.000 0.003 0.005 0.426 0.014 0.291 0.005 0.426 0.014 0.291 0.040											
BD Strawtinge 2021 BD 0.058 0.243 0.349 0.74 0.708 BD D 0.007 0.281 0.414 0.373 0.709 BD D 0.015 0.281 0.414 0.373 0.709 BD D 0.211 0.282 0.225 2.247 0.013 MDD Elderkin-Thompson 2012 MDD -0.250 0.216 0.085 1.986 0.986 0.986 MDD Goldsmith 2016 MDD -0.010 0.307 0.056 0.111 0.056 0.986 MDD Goldsmith 2016 MDD -0.110 0.307 0.056 0.116 0.281 0.286 MDD Goldsmith 2016 MDD -0.113 0.256 0.466 0.600 0.548 0.000 MDD Qu 2019 MDD -0.044 0.263 0.248 0.249 0.038 0.735 MDD MDD O.056 0.456 0.671 0.990 0.836 0.731 0.730 0.836 MDD Zhou 2021 SZ O.065											
BD Zazula 2021 BD 0.007 0.291 0.414 0.33 0.709 MDD Chang 2012 MDD 0.251 0.382 0.025 0.025 MDD Bohinska 2016 MDD 0.250 0.515 0.556 0.556 0.556 MDD Geldsmith 2016 MDD 0.210 0.327 0.203 0.214 0.086 0.956 MDD Geldsmith 2016 MDD 0.210 0.377 0.200 3.77 0.200 MDD Ail 2018 MDD 0.256 0.456 0.666 2.516 0.612 MDD Ye 2018 MDD 0.206 0.281 6.369 0.648 MDD Geldsmith 202 MDD 0.464 0.630 0.545 0.645 MDD Gelds 2020 MDD 0.046 0.673 8.73 0.000 MDD MDD 0.446 0.616 0.599 0.853 0.735 MDD MDD 0.046 0.077 2.561 0.041 0.347 0.729 MDD MDD <											
BD -0.065 -0.168 -0.020 -2.474 0.013 MDD Elderkin-Thompson 2012 MDD -0.250 -0.515 0.058 -1.19 MDD Bobinska 2016 MDD -0.250 -0.515 0.058 -1.19 MDD Goldsmith 2016 MDD -0.250 -0.515 0.058 -1.19 MDD Goldsmith 2016 MDD -0.520 -0.737 0.200 -0.779 0.000 MDD Saraykar 2018 MDD -0.150 0.268 -0.066 -0.616 0.012 MDD Qu 2019 MDD -0.464 -0.664 0.600 0.548 MDD Qu 2019 MDD -0.444 -0.239 -5.498 0.030 MDD Belge 2020 MDD 0.044 -0.239 -0.748 0.270 0.838 MDD MBD 0.133 -1.167 0.710 0.258 0.046 0.043 0.484 0.437 MDD Data 201 MDD 0.045 0.477 0.729 0.040 0.361 0.456 0.045 0.447											
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									-1.00	-0.50	0.00 0.50

Supplementary Figure 3: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and Cognitive Domain Attention for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Group by	Study name	Diagnosis	5	Statistics for each study					Corr	elation and 9	5% CI	
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value					
BD	Milton 2021	BD	0.127	0.065	0.188	3.969	0.000	1	1			
3D	Mora 2018	BD	0.108	-0.109	0.315	0.976	0.329			╶╶┼═╌	-	
3D	Millet 2019	BD	-0.115	-0.243	0.017	-1.709	0.087			-8 -∤		
D	Tseng 2019	BD	-0.048	-0.443	0.362	-0.220	0.826		—			
D	Vanden Ameele 2	021BD	-0.020	-0.259	0.221	-0.160	0.873			e		
D			0.025	-0.105	0.154	0.371	0.711					
IDD	Chang 2012	MDD	-0.195	-0.367	-0.010	-2.062	0.039		— —			
DD	Goldsmith 2016	MDD	-0.108	-0.305	0.098	-1.029	0.304		-	╼╉┼╾		
IDD	Samagula 2017	MDD	0.240	-0.125	0.548	1.295	0.195				╸	
IDD	Peters 2019	MDD	0.017	-0.296	0.327	0.103	0.918		-		-	
DD	Milton 2021	MDD	0.100	0.087	0.113	15.030	0.000					
IDD	Zhou 2021	MDD	0.018	-0.143	0.178	0.218	0.828					
DD			0.003	-0.117	0.123	0.043	0.965					
Z	Asevedo 2014	SZ	0.416	0.058	0.679	2.258	0.024			<u> </u>	e	
Z	Frydecka 2015	SZ	-0.143	-0.296	0.017	-1.752	0.080		- 1			
Ζ	Hori 2016	SZ	-0.010	-0.172	0.153	-0.120	0.905			+		
Z	de Campos-Carli	20 \$Z	0.316	0.005	0.571	1.990	0.047					
Z	Boozalis 2018	SZ	0.140	-0.184	0.436	0.846	0.398					
Z	Ergun 2018	SZ	0.020	-0.343	0.378	0.104	0.917		- I -			
Z	Kogan 2018	SZ	0.029	-0.323	0.374	0.158	0.875		-		_	
Z	Wilson 2018	SZ	-0.330	-0.732	0.243	-1.137	0.256	-	━┼╼		.	
Z	Fang 2019	SZ	-0.076	-0.222	0.074	-0.996	0.319					
Z	Fathian 2019	SZ	-0.380	-0.491	-0.257	-5.728	0.000		—			
Z	Malmqvist 2019	SZ	-0.119	-0.419	0.204	-0.717	0.473		—			
Z	Weiser 2019	SZ	-0.068	-0.166	0.032	-1.331	0.183			╼╾┼		
Z	Dal Santo 2020	SZ	-0.132	-0.296	0.040	-1.508	0.132		-	_ ∎		
Z	Klaus 2021	SZ	0.487	-0.011	0.792	1.919	0.055			- H		-
Ζ	North 2021	SZ	-0.146	-0.231	-0.059	-3.275	0.001					
Z	Zhang 2021	SZ	-0.358	-0.541	-0.143	-3.179	0.001		- +	-		
Z			-0.071	-0.164	0.022	-1.496	0.135					
Verall			-0.027	-0.091	0.037	-0.820	0.412			•		
								-1.00	-0.50	0.00	0.50	

Supplementary Figure 4: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and cognitive domain Language for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Group by	Study name	Diagnosis	5	Statistics	for each	study			Corr	elation and 9
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value			
BD	Lizano 2019	BD	-0.065	-0.205	0.078	-0.890	0.373		1	∎
BD	Sanchez-autet 201	BBD	-0.329	-0.441	-0.207	-5.080	0.000		│──■─	-
BD	Strawbridge 2021	BD	-0.031	-0.325	0.268	-0.199	0.843		- I	e
BD			-0.196	-0.283	-0.105	-4.198	0.000		•	
MDD	Bobinska 2016	MDD	-0.064	-0.269	0.146	-0.594	0.552		•	
MDD	Tateishi 2020	MDD	0.469	-0.182	0.834	1.439	0.150			
MDD			-0.015	-0.214	0.185	-0.149	0.882			
SZ	Frydecka 2015	SZ	-0.106	-0.261	0.055	-1.294	0.196		.	→ ∓
SZ	Zhang 2021	SZ	-0.354	-0.538	-0.138	-3.140	0.002		+	— I
SZ	Hori 2016	SZ	-0.020	-0.182	0.143	-0.239	0.811			_
SZ	de Campos-Carli 20) \$ Z	0.321	0.011	0.575	2.024	0.043			
SZ	Boozalis 2018	SZ	-0.300	-0.562	0.017	-1.857	0.063			
SZ	Ergun 2018	SZ	-0.088	-0.434	0.281	-0.458	0.647		I —	
SZ	Kudo 2018	SZ	0.140	-0.073	0.341	1.292	0.196			
SZ	Fang 2019	SZ	-0.062	-0.209	0.088	-0.812	0.417			
SZ	Fathian 2019	SZ	-0.350	-0.464	-0.225	-5.232	0.000		-	-
SZ	Lizano 2019	SZ	0.018	-0.114	0.149	0.260	0.795			-+
SZ	Malmqvist 2019	SZ	0.058	-0.262	0.367	0.348	0.728		- I -	
SZ	Weiser 2019	SZ	0.006	-0.094	0.106	0.121	0.903			_ + _
SZ	Borovcanin 2020	SZ	0.569	0.241	0.780	3.165	0.002			
SZ	Moustafa 2020	SZ	0.233	0.052	0.399	2.512	0.012			I —
SZ	King 2021	SZ	-0.079	-0.276	0.125	-0.759	0.448		-	<u> </u>
SZ	Orhan 2018	SZ	-0.380	-0.674	0.018	-1.876	0.061			
SZ			-0.047	-0.093	-0.001	-2.016	0.044			\bullet
Overall			-0.075	-0.115	-0.034	-3.631	0.000			\bullet
								-1.00	-0.50	0.00

1.00

Supplementary Figure 5: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and cognitive domain Processing Speed for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Group by	Study name	Diagnosis	S	Statistics	for each	study			Corr	elation and 95	% CI	
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value					
3D	Lizano 2019	BD	-0.065	-0.205	0.078	-0.890	0.373					
3D	Chakrabarty 2018	3 BD	-0.562	-0.725	-0.339	-4.405	0.000					
3D	Mora 2018	BD	0.065	-0.152	0.276	0.586	0.558				-	
BD	Millet 2019	BD	-0.185	-0.309	-0.055	-2.770	0.006		-	╼╾╴│		
3D	Strawbridge 2021	BD	0.149	-0.155	0.427	0.961	0.336				<u> </u>	
3D			-0.130	-0.318	0.067	-1.294	0.196					
1DD	Bobinska 2016	MDD	-0.034	-0.241	0.175	-0.315	0.752					
1DD	Goldsmith 2016	MDD	-0.110	-0.307	0.096	-1.048	0.295		-	╼╋┼╾		
1DD	Belge 2020	MDD	-0.044	-0.291	0.208	-0.338	0.735		- -			
1DD			-0.066	-0.191	0.062	-1.009	0.313					
Z	Frydecka 2015	SZ	-0.335	-0.470	-0.185	-4.239	0.000		- -	-		
Z	Boozalis 2018	SZ	0.000	-0.316	0.316	0.000	1.000		-	 	-	
Z	Ergun 2018	SZ	0.063	-0.304	0.414	0.328	0.743		-	<u>+</u> =	<u> </u>	
Z	Kogan 2018	SZ	-0.364	-0.632	-0.018	-2.054	0.040		_ 			
Z	Lizano 2019	SZ	0.018	-0.114	0.149	0.260	0.795			_ 		
Z	Malmqvist 2019	SZ	0.056	-0.264	0.365	0.336	0.737			-	-	
Z	Ribeiro-Santos 20	01892	-0.024	-0.270	0.225	-0.186	0.852		· · ·	-		
Z	Weiser 2019	SZ	0.066	-0.034	0.164	1.285	0.199			┼═─╴		
Z	Dal Santo 2020	SZ	-0.140	-0.304	0.032	-1.601	0.109		-	╼╾┼		
Z	De Picker 2020	SZ	-0.098	-0.369	0.188	-0.667	0.505		-			
Z	King 2021	SZ	-0.128	-0.322	0.077	-1.228	0.220		-	━━┼╴		
Z	Zhang 2021	SZ	-0.066	-0.288	0.164	-0.557	0.578		-			
Z			-0.080	-0.171	0.013	-1.695	0.090					
Overall			-0.082	-0.151	-0.012	-2.295	0.022			\bullet		
								-1.00	-0.50	0.00	0.50	

Group by	Study name	Diagnosis	5	Statistics	for each	study		Correlation and 95% Cl
Subgroup within study				Lower	Upper			
			Correlation	limit	limit	Z-Value	p-Value	
3D	Lizano 2019	BD	-0.078	-0.217	0.066	-1.062	0.288	
3D	Barbosa 2021	BD	0.500	0.131	0.747	2.576	0.010	
3D	Doganavsargil-Baysal 2	8613	-0.094	-0.353	0.178	-0.673	0.501	
3D	Chakrabarty 2018	BD	0.259	-0.018	0.499	1.836	0.066	│ │ ├──╋──┤ │
BD	Mora 2018	BD	0.061	-0.155	0.272	0.550	0.583	
BD	Millet 2019	BD	-0.236	-0.357	-0.108	-3.560	0.000	
3D	Tseng 2019	BD	-0.433	-0.717	-0.025	-2.073	0.038	
BD	Millet 2020	BD	-0.200	-0.324	-0.069	-2.980	0.003	
3D	Vanden Ameele 2020	BD	-0.030	-0.268	0.212	-0.240	0.810	
3D	Rahmani 2021	BD	0.430	0.051	0.701	2.206	0.027	
BD	Strawbridge 2021	BD	0.022	-0.277	0.317	0.141	0.888	
BD	Zazula 2021	BD	0.200	-0.166	0.518	1.073	0.283	
BD			0.002	-0.124	0.128	0.033	0.974	
MDD	Chang 2012	MDD	-0.227	-0.396	-0.043	-2.412	0.016	
NDD	Bobinska 2016	MDD	-0.163	-0.359	0.047	-1.525	0.127	
NDD	Samagula 2017	MDD	0.055	-0.305	0.402	0.291	0.771	
MDD	Ye 2018	MDD	0.120	-0.251	0.460	0.627	0.531	
MDD	Peters 2019	MDD	0.120	-0.231	0.519	1.534	0.125	
MDD	Tateishi 2020	MDD	-0.348	-0.784	0.319	-1.027	0.123	
MDD	Zhou 2021	MDD	-0.348	-0.178	0.318	-0.210	0.304	
	21100 2021							
MDD	1	07	-0.053	-0.183	0.079	-0.786	0.432	
SZ	Asevedo 2013	SZ	0.510	0.183	0.735	2.924	0.003	
SZ	Frydecka 2015	SZ	-0.257	-0.400	-0.101	-3.198	0.001	
SZ	Joseph 2015	SZ	-0.030	-0.238	0.181	-0.277	0.782	
SZ	Hori 2016	SZ	-0.025	-0.187	0.138	-0.299	0.765	
SZ	de Campos-Carli 2017	SZ	0.216	-0.102	0.494	1.335	0.182	
SZ	Boozalis 2018	SZ	0.010	-0.306	0.324	0.060	0.952	
SZ	Ergun 2018	SZ	-0.056	-0.408	0.311	-0.289	0.773	
SZ	Kogan 2018	SZ	-0.184	-0.501	0.176	-1.002	0.316	
SZ	Kudo 2018	SZ	0.030	-0.182	0.239	0.275	0.783	
SZ	Lizano 2019	SZ	-0.033	-0.163	0.099	-0.482	0.630	
SZ	Malmqvist 2019	SZ	0.111	-0.212	0.412	0.669	0.504	
SZ	Ribeiro-Santos 2019	SZ	-0.116	-0.354	0.136	-0.903	0.367	
SZ	Weiser 2019	SZ	-0.040	-0.139	0.060	-0.782	0.434	
SZ	Dal Santo 2020	SZ	-0.102	-0.268	0.070	-1.163	0.245	
SZ	Moustafa 2020	SZ	0.200	0.018	0.370	2.146	0.032	
SZ	King 2021	SZ	-0.194	-0.383	0.010	-1.864	0.062	
SZ	Klaus 2021	SZ	-0.167	-0.612	0.358	-0.608	0.543	
SZ	Zhang 2021	SZ	-0.031	-0.256	0.197	-0.263	0.792	
SZ			-0.026	-0.096	0.045	-0.712	0.476	
Overall			-0.025	-0.030	0.043	-0.882	0.470	
Jyeran			-0.025	-0.001	0.031	-0.002	0.570	-1.00 -0.50 0.00 0.50 1.00

Supplementary Figure 6: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and cognitive domain Reasoning for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Supplementary Figure 7: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and cognitive domain Verbal Memory for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

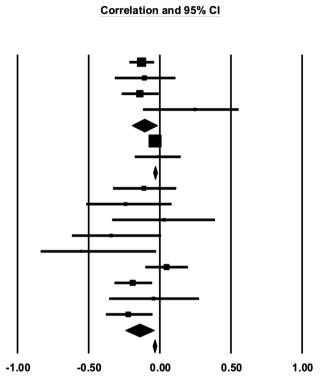
Group by	Study name	Diagnosis	s S	tatistics	for eac	у			Correlation and	
Subgroup within study					Upper					
			Correlation	limit	limit	Z-Value	p-Value			
BD	Lizano 2019	BD	-0.180	-0.314	-0.039	-2.489	0.013			
BD	Doganavsargil-Baysal 2013	BD	-0.121	-0.377	0.152	-0.868	0.385			
BD	Vinberg 2016	BD	-0.023	-0.318	0.276	-0.147	0.883			
BD	Mora 2018	BD	0.076	-0.141	0.286	0.685	0.493			+∎
BD	Sanchez-autet 2018	BD	-0.208	-0.330	-0.079	-3.138	0.002			
BD	Millet 2019	BD	-0.036	-0.167	0.096	-0.533	0.594			
BD	Vanden Ameele 2020	BD	-0.012	-0.251	0.229	-0.096	0.924			
BD	Strawbridge 2021	BD	0.083	-0.219	0.371	0.533	0.594			
BD			-0.085	-0.164	-0.005	-2.082	0.037			
MDD	Grassi-Oliveira 2011	MDD	-0.686	-0.839	-0.433	-4.367	0.000			
MDD	Elderkin-Thompson 2012	MDD	-0.340	-0.584	-0.040	-2.211	0.027			
MDD	Bobinska 2016	MDD	-0.111	-0.312	0.100	-1.034	0.301		1	╺──ॖॖॖॖॖॖॖॖॖॖੑ
MDD	Vinberg	MDD	0.019	-0.279	0.314	0.122	0.903			
MDD	Belge 2020	MDD	-0.044	-0.291	0.208	-0.338	0.735			
MDD	Zhou 2021	MDD	0.006	-0.155	0.167	0.077	0.938			
MDD			-0.186	-0.375	0.018	-1.785	0.074			
SZ	Martinez-Cengotitabengoa 2	0153Z	-0.382	-0.661	-0.010	-2.012	0.044			
SZ	Frydecka 2015	SZ	-0.261	-0.404	-0.106	-3.250	0.001		.	
SZ	Hori 2016	SZ	-0.045		0.118	-0.538	0.590			
SZ	Wu 2016	SZ	0.273	0.041	0.477	2.293	0.022			I-
SZ	de Campos-Carli 2017	SZ	0.421	0.126	0.648		0.006			
SZ	Boozalis 2018	SZ	-0.180	-0.469	0.144		0.275		I—	
SZ	Dorofeikova 2018	SZ	-0.280	-0.434	-0.110		0.001		-	
SZ	Ergun 2018	SZ		-0.350	0.371	0.062	0.950			
SZ	Kogan 2018	SZ	-0.134	-0.461	0.225		0.468		_	
SZ	Reboucas 2018	SZ		-0.181	0.470		0.355			
SZ	Wilson 2018	SZ		-0.186	0.759	1.335	0.182			
SZ	Xiu 2018	SZ	-0.250		0.091	-1.445	0.149			
SZ	Fang 2019	SZ	-0.054		0.096		0.480			_
SZ	Fathian 2019	SZ	-0.410		-0.290		0.000			— -
SZ	Lizano 2019	SZ	-0.053		0.079		0.431			
SZ	Malmqvist	SZ		-0.265	0.364		0.741			
SZ	Weiser 2019	SZ	-0.001	-0.203	0.098		0.980		1	
SZ	Borovcanin 2020	SZ	0.416	0.043	0.687	2.169	0.930		1	
SZ	Dal Santo 2020	SZ		-0.343	-0.013		0.030			
SZ	Miller 2020	SZ	-0.183	-0.665	-0.013		0.023			
SZ SZ	Moustafa 2020	SZ SZ	-0.408	-0.005	-0.060		0.023			_
SZ SZ	Zhang 2021	SZ SZ	-0.412		-0.204		0.010			-
SZ SZ		52	-0.412		0.030		0.000			
Overall			-0.072	-0.172		-1.377	0.168		1	
Overall			-0.089	-0.148	-0.029	-2.900	0.004	ا -1.00	l -0.50	0.00

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Supplementary Figure 8: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and cognitive domain Visual Memory for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Group by	Study name	Diagnosis	Statistics for each study								
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value				
BD	Milton 2021	BD	-0.128	-0.213	-0.041	-2.875	0.004				
BD	Mora 2018	BD	-0.108	-0.315	0.109	-0.976	0.329				
BD	Millet 2019	BD	-0.140	-0.267	-0.008	-2.086	0.037				
BD	Zazula 2021	BD	0.247	-0.118	0.553	1.335	0.182				
BD			-0.108	-0.196	-0.019	-2.379	0.017				
MDD	Milton 2021	MDD	-0.033	-0.046	-0.020	-4.945	0.000				
MDD	Zhou 2021	MDD	-0.015	-0.176	0.146	-0.184	0.854				
MDD			-0.033	-0.046	-0.020	-4.944	0.000				
SZ	Zhang 2013	SZ	-0.112	-0.328	0.115	-0.968	0.333				
SZ	Boozalis 2018	3 SZ	-0.240	-0.516	0.082	-1.469	0.142				
SZ	Ergun 2018	SZ	0.030	-0.334	0.386	0.156	0.876				
SZ	Kogan 2018	SZ	-0.342	-0.617	0.008	-1.919	0.055				
SZ	Wilson 2018	SZ	-0.550	-0.836	-0.027	-2.051	0.040				
SZ	Fang 2019	SZ	0.048	-0.101	0.195	0.628	0.530				
SZ	Fathian 2019	SZ	-0.190	-0.318	-0.055	-2.754	0.006				
SZ	Malmqvist 20	1 \$ 2	-0.044	-0.355	0.275	-0.266	0.790				
SZ	Dal Santo 202	20SZ	-0.221	-0.378	-0.052	-2.552	0.011				
SZ			-0.142	-0.241	-0.040	-2.724	0.006				
Overall			-0.036	-0.049	-0.023	-5.533	0.000				



Supplementary Figure 9: Forest Plot for correlation studies between Pro Inflammatory Index (PII) and cognitive domain Working Memory for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

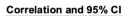
Group by	Study name	Diagnosis	5	for each	study			Correlation and 95% CI					
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value						
BD	Lizano 2019	BD	-0.093	-0.232	0.050	-1.275	0.202	1					
BD	Chakrabarty 2018	BD	-0.309	-0.539	-0.037	-2.213	0.027		+	<u> </u>			
3D	Millet 2019	BD	-0.214	-0.336	-0.085	-3.217	0.001			━─			
3D	Vanden Ameele 20	218D	-0.052	-0.289	0.191	-0.416	0.677		-				
3D	Strawbridge 2021	BD	-0.007	-0.303	0.291	-0.042	0.967		-		-		
3D	Zazula 2021	BD	-0.236	-0.545	0.129	-1.273	0.203			<u> </u>			
3D			-0.153	-0.231	-0.074	-3.744	0.000			◆			
MDD .	Ye 2018	MDD	0.110	-0.261	0.452	0.574	0.566						
//DD			0.110	-0.261	0.452	0.574	0.566						
SZ	Asevedo 2013	SZ	-0.400	-0.665	-0.046	-2.201	0.028						
SZ	Frydecka 2015	SZ	0.066	-0.095	0.223	0.804	0.421			_ +-			
Z	Hori 2016	SZ	-0.035	-0.196	0.128	-0.419	0.675						
SZ	de Campos-Carli 2	0 \$Z	0.235	-0.083	0.509	1.457	0.145						
SZ	Boozalis 2018	SZ	0.020	-0.297	0.333	0.120	0.904		-		-		
SZ	Ergun 2018	SZ	0.170	-0.203	0.500	0.892	0.372						
SZ	Kogan 2018	SZ	-0.055	-0.396	0.299	-0.296	0.767		—		-		
SZ	Kudo 2018	SZ	0.080	-0.133	0.286	0.735	0.462			_ 	-		
SZ	Lizano 2019	SZ	-0.048	-0.178	0.084	-0.713	0.476						
SZ	Malmqvist 2019	SZ	0.026	-0.292	0.339	0.156	0.876		-		-		
SZ	Ribeiro-Santos 201	96Z	-0.024	-0.270	0.225	-0.186	0.852		-	<u> </u>			
SZ	Dal Santo 2020	SZ	-0.107	-0.273	0.065	-1.220	0.222		-				
SZ	De Picker 2020	SZ	-0.120	-0.388	0.167	-0.818	0.413						
SZ	Moustafa 2020	SZ	0.240	0.060	0.405	2.590	0.010				<u> </u>		
SZ	Klaus 2021	SZ	-0.500	-0.798	-0.006	-1.981	0.048		_				
SZ	Zhang 2021	SZ	0.036	-0.193	0.261	0.306	0.760				.		
SZ	-		0.002	-0.071	0.076	0.066	0.947			•			
Overall			-0.065	-0.118	-0.011	-2.363	0.018			•			
								-1.00	-0.50	0.00	0.50	1	

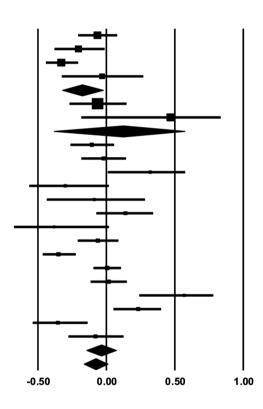
Supplementary Figure 10: Forest Plot for correlation studies between Anti Inflammatory Index (AII) and Global Cognition for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Study name	Diagnosis	; S	Statistics	for eac	h study			Correla	ation and	95% CI	
		Correlation	Lower limit	Upper limit	Z-Value	p-Value					
Xiu 2016	SZ	0.217	0.045	0.376	2.465	0.014				┣╴│	
Klaus 2021	SZ	-0.072	-0.548	0.439	-0.260	0.795					
Belge 2020	MDD	-0.159	-0.393	0.095	-1.232	0.218			∎┼		
Strawbridge 202	21 BD	0.143	-0.161	0.422	0.919	0.358					
Frydecka 2015	SZ	0.053	-0.104	0.207	0.660	0.509			-#		
		0.067	-0.069	0.201	0.966	0.334			•		
							-1.00	-0.50	0.00	0.50	1.00

Supplementary Figure 11: Forest Plot for correlation studies between Anti Inflammatory Index (AII) and Cognitive Domain Language for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Group by	Study name	Diagnosis	9	Statistics	for each	study		
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value	
BD	Lizano 2019	BD	-0.065	-0.205	0.078	-0.890	0.373	
BD	Dickerson 2013	BD	-0.204	-0.379	-0.014	-2.105	0.035	
BD	Sanchez-autet 201	8BD	-0.329	-0.441	-0.207	-5.080	0.000	
BD	Strawbridge 2021	BD	-0.031	-0.325	0.268	-0.199	0.843	
BD	-		-0.177	-0.322	-0.024	-2.266	0.023	
MDD	Bobinska 2016	MDD	-0.064	-0.269	0.146	-0.594	0.552	
MDD	Tateishi 2020	MDD	0.469	-0.182	0.834	1.439	0.150	
MDD			0.123	-0.383	0.572	0.459	0.646	
SZ	Frydecka 2015	SZ	-0.106	-0.261	0.055	-1.294	0.196	
SZ	Hori 2016	SZ	-0.020	-0.182	0.143	-0.239	0.811	
SZ	de Campos-Carli 2	20 SZ	0.321	0.011	0.575	2.024	0.043	
SZ	Boozalis 2018	SZ	-0.300	-0.562	0.017	-1.857	0.063	
SZ	Ergun 2018	SZ	-0.088	-0.434	0.281	-0.458	0.647	
SZ	Kudo 2018	SZ	0.140	-0.073	0.341	1.292	0.196	
SZ	Orhan 2018	SZ	-0.380	-0.674	0.018	-1.876	0.061	
SZ	Fang 2019	SZ	-0.062	-0.209	0.088	-0.812	0.417	
SZ	Fathian 2019	SZ	-0.350	-0.464	-0.225	-5.232	0.000	
SZ	Weiser 2019	SZ	0.006	-0.094	0.106	0.121	0.903	
SZ	Lizano 2019	SZ	0.018	-0.114	0.149	0.260	0.795	
SZ	Borovcanin 2020	SZ	0.569	0.241	0.780	3.165	0.002	
SZ	Moustafa 2020	SZ	0.233	0.052	0.399	2.512	0.012	
SZ	Zhang 2021	SZ	-0.354	-0.538	-0.138	-3.140	0.002	
SZ	King 2021	SZ	-0.079	-0.276	0.125	-0.759	0.448	
SZ			-0.037	-0.145	0.071	-0.673	0.501	
Overall			-0.078	-0.165	0.009	-1.750	0.080	
								-1.00





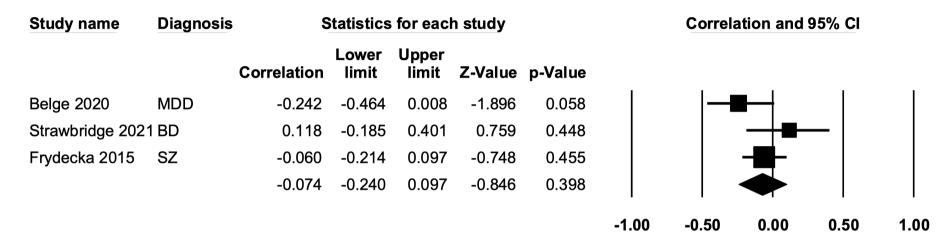
Supplementary Figure 12: Forest Plot for correlation studies between Anti Inflammatory Index (AII) and Cognitive Domain Processing Speed for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Study name	Diagnosis	s S	Statistics	for eacl	h study			Correla	ation and	95% CI	
		Correlation	Lower limit	Upper limit	Z-Value	p-Value					
Moustafa 2020	SZ	0.251	0.071	0.415	2.714	0.007				┣━│	
Goldsmith 2016	MDD	0.210	0.007	0.397	2.022	0.043				┣━│	
Belge 2020	MDD	-0.075	-0.319	0.178	-0.579	0.562		-			
Strawbridge 202	1 BD	0.011	-0.287	0.307	0.070	0.944		-		-	
		0.125	-0.030	0.275	1.587	0.113				•	
							-1.00	-0.50	0.00	0.50	1.00

Supplementary Figure 13: Forest Plot for correlation studies between Anti Inflammatory Index (AII) and Cognitive Domain Reasoning for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Study name	Diagnosis	; S	Statistics	for eacl	h study			Correla	ation and	95% Cl	
		Correlation	Lower limit	Upper limit	Z-Value	p-Value					
Klaus 2021	SZ	-0.243	-0.659	0.287	-0.894	0.371			∎┼──	-	
Samagula 2017	MDD	-0.173	-0.497	0.193	-0.925	0.355			╉┼─		
Strawbridge 202	1 BD	-0.061	-0.352	0.240	-0.391	0.696		-	╶╋──		
Frydecka 2015	SZ	0.230	0.077	0.373	2.916	0.004			-	┣╴│	
		-0.002	-0.245	0.241	-0.019	0.985			\blacklozenge		
							-1.00	-0.50	0.00	0.50	1.00

Supplementary Figure 14: Forest Plot for correlation studies between Anti Inflammatory Index (AII) and Cognitive Domain Verbal Memory for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))



Supplementary Figure 15: Forest Plot for correlation studies between C Reactive Protein (CRP) and Global Cognition for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Froup by	Study name	Diagnosis	S	tatistics	for each	study		
ubgroup within study				Lower	Upper			
			Correlation	limit	limit	Z-Value	p-Value	
D	Lizano 2019	BD	-0.220	-0.351	-0.080	-3.058	0.002	
D	Millet 2019	BD	-0.130	-0.257	0.002	-1.935	0.053	
D	Milton 2021	BD	0.000	-0.063	0.063	0.000	1.000	
D	Sanchez-autet 20	01 B D	-0.270	-0.387	-0.144	-4.116	0.000	
D	Strawbridge 202	1 BD	-0.019	-0.314	0.280	-0.120	0.905	
D	Tanaka 2017	BD	-0.001	-0.350	0.348	-0.005	0.996	
D	Tseng 2016	BD	-0.251	-0.594	0.170	-1.175	0.240	
D	Vanden Ameele	2012210	-0.075	-0.310	0.168	-0.601	0.548	
D			-0.126	-0.225	-0.024	-2.412	0.016	
1DD	Belge 2020	MDD	-0.226	-0.451	0.025	-1.769	0.077	
1DD	Milton 2021	MDD	0.009	-0.005	0.022	1.273	0.203	
1DD	Qu 2019	MDD	-0.330	-0.491	-0.147	-3.445	0.001	
1DD	Zhou 2021	MDD	0.058	-0.104	0.217	0.702	0.483	
1DD			-0.103	-0.264	0.062	-1.223	0.221	
Z	Boozalis 2018	SZ	-0.030	-0.342	0.288	-0.180	0.857	
Z	Dal Santo 2020	SZ	-0.162	-0.323	0.010	-1.850	0.064	
Z	Fathian 2019	SZ	-0.370	-0.482	-0.246	-5.561	0.000	
Z	Frydecka 2015	SZ	0.050	-0.111	0.208	0.609	0.543	
Z	Johnsen 2016	SZ	-0.247	-0.406	-0.074	-2.774	0.006	
Z	Klaus 2021	SZ	-0.198	-0.632	0.330	-0.723	0.469	
Z	Lizano 2019	SZ	-0.080	-0.209	0.052	-1.189	0.234	
Z	Lizano 2020	SZ	-0.216	-0.369	-0.052	-2.569	0.010	
SZ	Weiser 2019	SZ	0.008	-0.091	0.108	0.165	0.869	
SZ			-0.139	-0.245	-0.030	-2.489	0.013	
)verall			-0.127	-0.194	-0.059	-3.658	0.000	
								-1.00

Supplementary Figure 16: Forest Plot for correlation studies between IFN-g and Global Cognition for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Study name	Diagnosis	s S	tatistics	for eac	h study		Correlation and 95% CI					
		Correlation		Upper limit	Z-Value	p-Value						
Belge	MDD	0.139	-0.115	0.376	1.075	0.283			╶┼┲	—		
Wilson	SZ	-0.390	-0.763	0.177	-1.366	0.172		╶─┤■				
Klaus 2021	SZ	-0.295	-0.690	0.235	-1.096	0.273		─┼╼				
Strawbridge 2021	BD	0.140	-0.164	0.419	0.902	0.367						
Vanden Ameele 202	21 BD	0.121	-0.123	0.351	0.973	0.331			╶┼╋╋			
		0.055	-0.112	0.219	0.647	0.517						
							-1.00	-0.50	0.00	0.50	1.	

Supplementary Figure 17: Forest Plot for correlation studies between IL-1b and Global Cognition for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

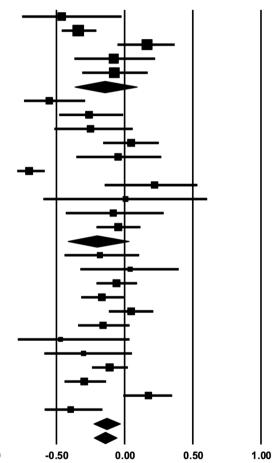
Group by	Study name	Diagnosis		Statistics	for each	study		Correlation and 95% CI					
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value						
BD	Lizano 2019	BD	-0.100	-0.239	0.043	-1.372	0.170			■+			
BD			-0.100	-0.239	0.043	-1.372	0.170						
MDD	Belge 2020	MDD	0.076	-0.177	0.320	0.585	0.559				_		
MDD	Goldsmith 20	16/1DD	-0.004	-0.208	0.200	-0.040	0.968						
MDD	Qu 2019	MDD	-0.290	-0.457	-0.103	-3.001	0.003			_			
MDD	Tateishi 2020	MDD	0.050	-0.567	0.631	0.142	0.887		_				
MDD	Zhou 2021	MDD	0.078	-0.084	0.236	0.944	0.345			+=			
MDD			-0.035	-0.198	0.130	-0.416	0.677						
SZ	De Picker 202	2 (\$Z	-0.124	-0.392	0.163	-0.845	0.398						
SZ	Kogan 2018	SZ	-0.186	-0.502	0.174	-1.013	0.311						
SZ	Lizano 2019	SZ	-0.020	-0.151	0.112	-0.297	0.767						
SZ	Zhang 2021	SZ	-0.296	-0.490	-0.074	-2.589	0.010		=	<u> </u>			
SZ			-0.131	-0.270	0.013	-1.789	0.074		-				
Overall			-0.094	-0.179	-0.007	-2.122	0.034						
								-1.00	-0.50	0.00	0.50	1	

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Supplementary Figure 18: Forest Plot for correlation studies between IL-6 and Global Cognition for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Group by	Study name	Diagnosis	Statistics for each study			study		
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value	
BD	Barbosa 2018	BD	-0.461	-0.750	-0.023	-2.056	0.040	I
BD	Lizano 2019	BD	-0.340	-0.460	-0.208	-4.842	0.000	
BD	Mora 2018	BD	0.165	-0.051	0.366	1.499	0.134	
BD	Strawbridge 2021	BD	-0.080	-0.368	0.223	-0.510	0.610	
BD	vanden Ameele 202	1 BD	-0.075	-0.310	0.168	-0.604	0.546	
BD			-0.146	-0.365	0.089	-1.217	0.224	
MDD	Ali 2018	MDD	-0.552	-0.737	-0.290	-3.779	0.000	
MDD	Belge 2020	MDD	-0.261	-0.479	-0.012	-2.049	0.040	
MDD	Elderkin-Thompson 2	20 1112 D	-0.250	-0.515	0.058	-1.595	0.111	
MDD	Goldsmith 2016	MDD	0.049	-0.157	0.250	0.460	0.645	
MDD	Peters 2019	MDD	-0.048	-0.354	0.268	-0.289	0.772	
MDD	Qu 2019	MDD	-0.700	-0.787	-0.586	-8.716	0.000	
MDD	Samagula 2017	MDD	0.220	-0.146	0.533	1.183	0.237	
MDD	Tateishi 2020	MDD	0.007	-0.595	0.604	0.020	0.984	
MDD	Ye 2018	MDD	-0.083	-0.430	0.286	-0.432	0.666	
MDD	Zhou 2021	MDD	-0.046	-0.206	0.115	-0.561	0.575	
MDD			-0.203	-0.416	0.030	-1.708	0.088	
SZ	De Picker 2020	SZ	-0.181	-0.440	0.106	-1.241	0.215	
SZ	Ergun 2018	SZ	0.041	-0.324	0.395	0.213	0.831	
SZ	Fang 2019	SZ	-0.059	-0.206	0.091	-0.772	0.440	
SZ	Frydecka 2015	SZ	-0.167	-0.318	-0.007	-2.046	0.041	
SZ	Hori 2016	SZ	0.049	-0.115	0.209	0.580	0.562	
SZ	King 2021	SZ	-0.158	-0.340	0.036	-1.601	0.109	
SZ	Klaus 2021	SZ	-0.469	-0.783	0.035	-1.834	0.067	
SZ	Kogan 2018	SZ	-0.301	-0.588	0.053	-1.673	0.094	
SZ	Lizano 2019	SZ	-0.110	-0.238	0.022	-1.638	0.101	
SZ	Lizano 2020	SZ	-0.296	-0.440	-0.137	-3.571	0.000	
SZ	Moustafa 2020	SZ	0.175	-0.008	0.347	1.871	0.061	
SZ	Ribeiro-Santos 2019	SZ	-0.395	-0.585	-0.163	-3.236	0.001	ľ
SZ			-0.131	-0.227	-0.034	-2.635	0.008	
Overall			-0.143	-0.224	-0.059	-3.320	0.001	ſ
								-1.

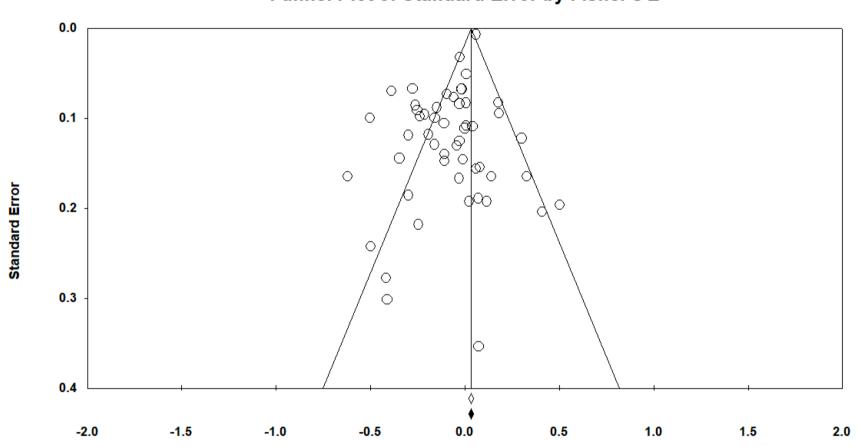
Correlation and 95% CI



Supplementary Figure 19: Forest Plot for correlation studies between TNF-a and Global Cognition for all studies, as well as diagnostic subgroups (Bipolar Disorder (BD), Major Depressive Disorder (MDD), and schizophrenia spectrum disorders (SZ))

Group by	Study name	Diagnosis	S	tatistics	for each	study			Corr	elation and 9	5% CI	
Subgroup within study			Correlation	Lower limit	Upper limit	Z-Value	p-Value					
BD	Chakrabarty 2018	BD	-0.333	-0.557	-0.063	-2.399	0.016			<u> </u>		
BD	Doganavsargil-Baysal	268133	-0.128	-0.383	0.145	-0.919	0.358		I —			
BD	Lizano 2019	BD	0.150	0.008	0.286	2.067	0.039			┝──╋─	-	
BD	Millet 2020	BD	-0.006	-0.138	0.127	-0.088	0.930			_ 		
BD	Mora 2018	BD	0.038	-0.178	0.250	0.342	0.732				.	
BD	Strawbridge 2021	BD	0.025	-0.274	0.319	0.157	0.875		·	e	_	
BD	vanden Ameele 2021	BD	-0.057	-0.293	0.186	-0.454	0.650		-	_		
BD			-0.018	-0.127	0.091	-0.329	0.742					
MDD	Belge 2020	MDD	-0.127	-0.365	0.127	-0.982	0.326		I —	━━━━━━━━		
MDD	Bobinska 2016	MDD	-0.093	-0.296	0.118	-0.865	0.387		- 1	∎		
MDD	Goldsmith 2016	MDD	-0.028	-0.231	0.176	-0.269	0.788					
MDD	Peters 2019	MDD	0.120	-0.199	0.416	0.733	0.463					
MDD	Tateishi 2020	MDD	0.083	-0.544	0.650	0.235	0.814			-		
MDD	Zhou 2021	MDD	0.001	-0.160	0.162	0.009	0.993					
MDD			-0.030	-0.125	0.065	-0.624	0.533			-		
SZ	Amin 2020	SZ	-0.011	-0.288	0.268	-0.075	0.940		-		-	
SZ	De Picker 2020	SZ	-0.059	-0.335	0.226	-0.401	0.689			e		
SZ	Ergun 2018	SZ	0.022	-0.341	0.379	0.114	0.909		_			
SZ	Hori 2016	SZ	-0.046	-0.207	0.117	-0.550	0.582					
SZ	Klaus 2021	SZ	-0.610	-0.849	-0.164	-2.556	0.011	_		-		
SZ	Kogan 2018	SZ	-0.303	-0.589	0.051	-1.685	0.092					
SZ	Lizano 2019	SZ	-0.060	-0.190	0.072	-0.891	0.373					
SZ	Ribeiro-Santos 2019	SZ	0.100	-0.152	0.339	0.777	0.437				— I	
SZ	Zazula 2021	SZ	-0.033	-0.382	0.326	-0.172	0.863		I —	e	-	
SZ	Zhang 2021	SZ	-0.027	-0.252	0.201	-0.229	0.819			e		
SZ	5		-0.055	-0.131	0.022	-1.403	0.160					
Overall			-0.039	-0.091	0.013	-1.459	0.144					
								-1.00	-0.50	0.00	0.50	1.00

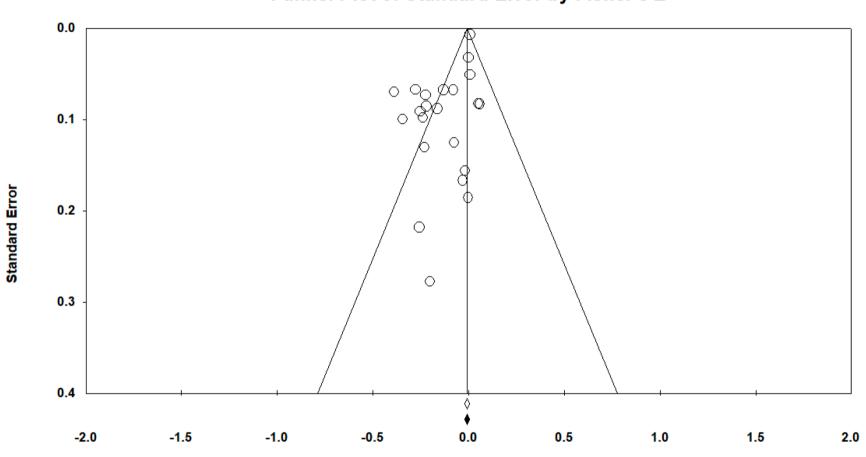
Supplementary Figure 20: Funnel Plot Correlation studies of Pro Inflammatory Index (PII) with Global Cognition



Funnel Plot of Standard Error by Fisher's Z

Fisher's Z

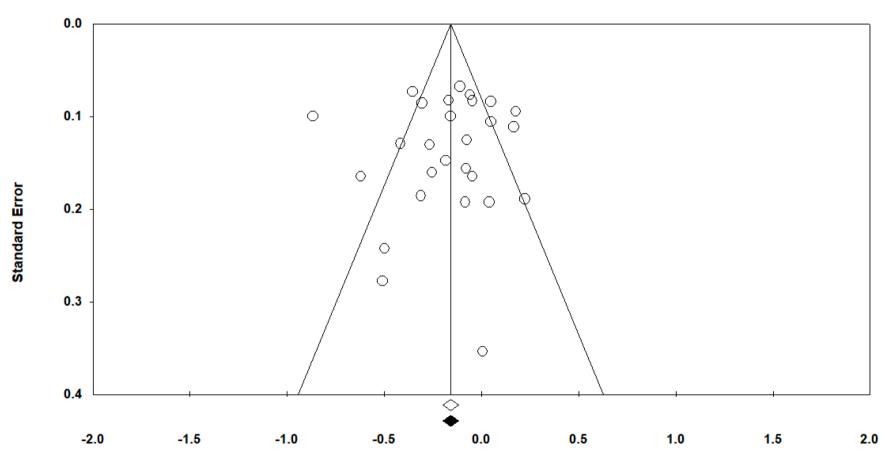
Supplementary Figure 21: Funnel Plot Correlation Studies CRP with Global Cognition



Funnel Plot of Standard Error by Fisher's Z

Fisher's Z

Supplementary Figure 22: Funnel Plot Correlation Studies IL-6 with Global Cognition



Funnel Plot of Standard Error by Fisher's Z

Fisher's Z

Supplementary document: Protocol (12/9/2021) + Update to protocol 4/1/2022 (PROSPERO) + Final Protocol (version 4/1/2022)

Supplementary document: Protocol : The relationship between immune and cognitive dysfunction in mood and psychotic disorder: a systematic review and a meta-analysis

Submitted PROSPERO: 12/9/2021

The current meta-analysis aims to evaluate the presence of an association between immune-related aberrances and neuropsychological deficits in mood and psychotic disorders. The impact of reporting and publication bias will be evaluated.

Review Questions

- 1) Are neuropsychological deficits associated to centrally assessed immune-related biomarkers in mood and psychotic disorder?
- 2) Are neuropsychological deficits associated to peripherally assessed immune-related biomarkers in mood and psychotic disorders?
- 3) If present, are these associations different in mood versus psychotic disorders?
- 4) Are these associations moderated by publication year, age, duration of illness, gender, smoking status or BMI?

Studies included in the review:

- Cross-sectional or longitudinal studies in peer reviewed journals
- Studies investigating a patient group with either psychotic or mood disorder, i.e. Primary diagnosis of Schizophrenia, schizophreniform disorder, Schizoaffective disorder, Psychotic disorder NOS, Brief Psychotic Disorder, Major Depressive disorder, Bipolar Disorder, Dysthymia
- Inclusion of at least 1 neuropsychological measure (NP)
- Inclusion of at least 1 immune-related marker (IM)

Exclusion criteria

- Case reports, case series
- Abstracts, conference proceedings
- Systematic review, narrative review
- Opinion paper
- Meta-analysis

Search strategy

platform	Search strategy
Pubmed	(schizophreni* OR schizoaffective OR psychotic OR psychosis OR MDD OR "depressive disorder" OR "major depression" OR manic OR mania OR bipolar OR "mood disorder" OR "affective disorder" OR dysthym*) AND (immun* OR chemokine* OR cytokine* OR interleukin* OR CRP OR C- reactive OR IL-1b OR IL-1β OR IL-1ra OR IL-2 OR IL-4 OR IL-6 OR IL-8 OR IL-10 OR IL-12 OR "tumor necrosis factor" OR TNF OR IFN OR IFN-γ OR Interferon* OR kynuren* OR quinolinic OR xanthurenic OR picolinic OR anthranilic OR HLA OR lymphocyt* OR monocyt* OR Leukocyt* OR neutrophil* OR basophil* or eosinophil*) AND (cogniti* OR attenti* OR vigilan* OR "executive functioning" OR reasoning OR "problem solving" OR memory OR learning OR "processing speed") NOT (review [Publication type])
Web of	(ALL=(schizophreni*) OR ALL=(schizoaffective) OR ALL=(psychotic) OR ALL=(psychosis) OR ALL=(MDD) OR ALL=(depressive disorder) OR
Science	ALL=(major depression) OR ALL=(manic) OR ALL=(mania) OR ALL=(bipolar) OR ALL=(mood disorder) OR ALL=(affective disorder) OR ALL=(dysthym*)) AND (ALL=(immun*) OR ALL=(chemokine*) OR ALL=(cytokine*) OR ALL=(interleukin*) OR ALL=(CRP) OR ALL=(C-reactive) OR ALL=(IL-1b) OR ALL=(IL-1β) OR ALL=(IL-1ra) OR ALL=(IL-2) OR ALL=(IL-4) OR ALL=(IL-6) OR ALL=(IL-8) OR ALL=(IL-10) OR ALL=(IL-12) OR ALL=(tumor necrosis factor) OR ALL=(TNF) OR ALL=(IFN) OR ALL=(IFN-γ) OR ALL=(Interferon*) OR ALL=(kynuren*) OR ALL=(quinolinic) OR ALL=(xanthurenic) OR ALL=(picolinic) OR ALL=(anthranilic) OR ALL=(HLA) OR ALL=(lymphocyt*) OR ALL=(monocyt*) OR ALL=(leukocyt*) OR ALL=(neutrophil*) OR ALL=(basophil*) OR ALL=(eosinophil*)) AND (ALL=(cognitive*) OR ALL=(attenti*) OR ALL=(vigilan*) OR ALL=(executive functioning) OR ALL=(reasoning) OR ALL=(problem solving) OR ALL=(memory) OR ALL=(learning) OR ALL=(processing speed))
Psycinfo	Any Field: schizophrenia <i>OR</i> Any Field: schizophreniform <i>OR</i> Any Field: psychotic <i>OR</i> Any Field: psychosis <i>OR</i> Any Field: MDD <i>OR</i> Any Field: depressive disorder <i>OR</i> Any Field: major depression <i>OR</i> Any Field: manic <i>OR</i> Any Field: mania <i>OR</i> Any Field: bipolar <i>OR</i> Any Field: major depression <i>OR</i> Any Field: manic <i>OR</i> Any Field: mania <i>OR</i> Any Field: bipolar <i>OR</i> Any Field: mood disorder <i>OR</i> Any Field: affective disorder <i>OR</i> Any Field: dysthymia <i>AND</i> Any Field: Immune OR cytokine OR chemokine OR interleukin OR CRP OR IL-1b OR IL-1β OR IL-1ra OR IL-2 OR IL-4 OR IL-6 OR IL-8 OR IL-10 OR IL-12 OR tumor necrosis factor OR TNF OR IFN OR IFN-γ OR Interferon OR kynurenine OR kynurenic OR quinolinic OR xanthurenic OR picolinic OR any Field: cognitive <i>OR</i> Any Field: vigilance <i>OR</i> Any Field: executive function <i>OR</i> Any Field: executive functioning <i>OR</i> Any Field: problem solving <i>OR</i> Any Field: memory <i>OR</i> Any Field: learning <i>OR</i> Any Field: processing speed <i>AND</i> Peer-Reviewed Journals only

Main outcome measure:

A correlation value (pearson's r or rho value) or regression coefficient (B value) reporting on the association between neuropsychological measure(s) (NP) and immune-related marker(s) (IM)

Data extraction:

Two reviewers (MM and CO) will independently evaluate the search results. Title and abstract of all search hits will be evaluated based on inclusion and exclusion criteria. Relevant or potentially relevant papers will be extracted:

- author, publication year, diagnosis, sample size, mean age, mean DOI, gender ratio, %smoking, mean BMI, name of cognitive domain, name of cognitive test, immune biomarker, tissue (serum, plasma, CSF, tracer, cells), bioanalytical method - correlation (pearson's r or rho value) or regression coefficient (B value) between neuropsychological measure(s) and immune-related biomarker(s), p-value.

- Number of neuropsychological tests included in the study

- number of immune biomarkers included in the study

- number of reported correlations

Data will be recorded in excel sheet.

Investigated cognitive domains and cognitive tests included

Domain	Tests
Verbal learning and memory	List learning tasks (RBANS-memory, BACS, CVLT, RaVLT,)
Visual learning and memory	RBANS-visuospatial; pairs matching test;
Working memory	LNS, Letter sequencing, Digit backward, spatial span test, Digit
	sequencing test, BACS-WM, MCCB-WM, delayed match to sample test,
Attention and vigilance	RBANS-attention, MCCB-attention, BACS-attention, CANTAB-attention,
	CPT, Digit span, simple reaction time
Processing speed	Digit Symbol Coding tests, TMTB
Reasoning and problem	WCST, Tower of London, CANTAB-set shift, Stroop test, Mazes, BACS-
solving	EF, abstraction test, matrix reasoning, MCCB reasoning,
Language	RBANS-language, Verbal Fluency tests, COWAT, naming test

When in a single study more than one IM is correlated to a specific cognitive domain on a composite score will be calculated (based on FIsher's z transformation of the r values), resulting in a single r score reflecting the association of the merged correlational values between the cognitive domain and the pro-inflammatory and anti-inflammatory markers.

Authors of the papers with missing results will be contacted. In case of non-response, a reminder will be sent.

Risk of Bias Assessment:

Biocross will be used to assess the quality of the studies

Strategy for meta-analysis

- Comprehensive Meta Analysis (CMA) will be used for the meta-analysis.
- Correlation and 95% CI as well as Z-value and p value will be reported per study, as well as for the overall summary of the random model
- Analyses will be performed for:
 - Psychotic and mood disorders combined, as well as for three diagnostic groups separately (SZ, BD, MDD)
 - For pro-inflammatory markers combined
 - o For anti-inflammatory markers combined
 - For biomarkers that have been investigated in at least three different, independent studies in the same diagnosis (e.g. CRP, IL-6, IL-1b) for the same cognitive domain, separate meta-analyses will be performed

Update to protocol 4/1/2022

Review Question

Given that MDD and BD should be evaluated as separate diagnoses, rather than a group of 'mood disorders', we chose to separately analyze these diagnostic groups, rather than lumping them together

Research question 3 was adapted: "If present, are these associations different in mood versus psychotic disorders?"

was adjusted into

"Are those associations different between Schizophrenia (SZ), Major Depressive Disorder (MDD) and Bipolar Disorder (BD)?"

Main outcome(s)

The following analyses were already described in the analyses plan of the original PROSPERO registration, but we chose to clarify how the pro-inflammatory index (PII) and Anti-inflammatory Index (AII) were calculated. Therefore we added the following passage in the updated registration.

The following passage needs to be added:

"The primary Immunomarker (IM) outcome variables will be two composite inflammatory indices

- Pro-inflammatory Index, PII
- Anti-Inflammatory Index, All

If only a single IM is included in the study, that IM x Neuropsychological measure correlation coefficient will be used for the PII/AII associations. If more IM are included, PII and AII will be calculated for each cognitive domain, averaging out the associations between that specific cognitive domain on one hand and the available immunomarker-based correlations on the other (based on Fisher's z transformation of the r values)."

"Primary outcome of the study is PII/AII x composite score for all combined diagnoses.

PII/AII x individual cognitive domains for combined diagnosis and the separate diagnoses (SZ, MDD, BD) will also be calculated and reported"

Additional outcomes

The following analyses were performed as secondary outcome analyses

"Secondary IM outcome variables are individual IM when >3 studies are available.

In case of a significant association, exploratory subgroup analyses will be performed to define which of the diagnoses contributes to the statistically significant association."

Risk of bias (quality) assessment

Because the majority of the studies were cross-sectional studies, GRADE could not be used as a tool for Quality Assessment. Therefore, we chose the more appropriate tool BIOCROSS.

"Quality assessment of eligible papers was performed with the BIOCROSS evaluation tool, which is specifically developed for biomarker-based crosssectional studies."

Analysis of subgroups or subsets In line with the adjustments made in RQ3

Three patient subgroups will be analyzed:

- all diagnoses combined
- psychotic disorders and mood disorders separately

Was changed into

Three patient subgroups will be analyzed:

- all diagnoses combined
- Schizophrenia, Major Depressive Disorder and Bipolar Disorder separately

Supplementary document: Final Protocol : The relationship between immune and cognitive dysfunction in mood and psychotic disorder: a systematic review and a meta-analysis PROSPERO 2021 CRD42021278371

Version 4/1/2022

The current meta-analysis aims to evaluate the presence of an association between immune-related aberrances and neuropsychological deficits in mood and psychotic disorders. The impact of reporting and publication bias will be evaluated.

Review Questions

- 5) Are neuropsychological deficits associated to centrally assessed immune-related biomarkers in mood and psychotic disorder?
- 6) Are neuropsychological deficits associated to peripherally assessed immune-related biomarkers in mood and psychotic disorders?
- 7) Are those associations different between Schizophrenia (SZ), Major Depressive Disorder (MDD) and Bipolar Disorder (BD)?"
- 8) Are these associations moderated by publication year, age, duration of illness, gender, smoking status or BMI?

Studies included in the review:

- Cross-sectional or longitudinal studies in peer reviewed journals
- Studies investigating a patient group with either psychotic or mood disorder, i.e. Primary diagnosis of Schizophrenia, schizophreniform disorder, Schizoaffective disorder, Psychotic disorder NOS, Brief Psychotic Disorder, Major Depressive disorder, Bipolar Disorder, Dysthymia
- Inclusion of at least 1 neuropsychological measure (NP)
- Inclusion of at least 1 immune-related marker (IM)

Exclusion criteria

- Case reports, case series
- Abstracts, conference proceedings
- Systematic review, narrative review
- Opinion paper
- Meta-analysis

Search strategy

platform	Search strategy
Pubmed	(schizophreni* OR schizoaffective OR psychotic OR psychosis OR MDD OR "depressive disorder" OR "major depression" OR manic OR mania OR bipolar OR "mood disorder" OR "affective disorder" OR dysthym*) AND (immun* OR chemokine* OR cytokine* OR interleukin* OR CRP OR C-reactive OR IL-1b OR IL-1β OR IL-1ra OR IL-2 OR IL-4 OR IL-6 OR IL-8 OR IL-10 OR IL-12 OR "tumor necrosis factor" OR TNF OR IFN OR IFN-γ OR Interferon* OR kynuren* OR quinolinic OR xanthurenic OR picolinic OR anthranilic OR HLA OR lymphocyt* OR monocyt* OR Leukocyt* OR neutrophil* OR basophil* or eosinophil*) AND (cogniti* OR attenti* OR vigilan* OR "executive functioning" OR reasoning OR "problem solving" OR memory OR learning OR "processing speed") NOT (review [Publication type])
Web of Science	 (ALL=(schizophreni*) OR ALL=(schizoaffective) OR ALL=(psychotic) OR ALL=(psychosis) OR ALL=(MDD) OR ALL=(depressive disorder) OR ALL=(major depression) OR ALL=(manic) OR ALL=(mania) OR ALL=(bipolar) OR ALL=(mood disorder) OR ALL=(affective disorder) OR ALL=(dysthym*)) AND (ALL=(immun*) OR ALL=(chemokine*) OR ALL=(cytokine*) OR ALL=(interleukin*) OR ALL=(CRP) OR ALL=(C-reactive) OR ALL=(IL-1b) OR ALL=(IL-1β) OR ALL=(IL-1ra) OR ALL=(IL-2) OR ALL=(IL-4) OR ALL=(IL-6) OR ALL=(IL-8) OR ALL=(IL-10) OR ALL=(IL-12) OR ALL=(tumor necrosis factor) OR ALL=(TNF) OR ALL=(IFN) OR ALL=(IFN-γ) OR ALL=(Interferon*) OR ALL=(kynuren*) OR ALL=(quinolinic) OR ALL=(xanthurenic) OR ALL=(picolinic) OR ALL=(anthranilic) OR ALL=(ILAA) OR ALL=(Iymphocyt*) OR ALL=(monocyt*) OR ALL=(leukocyt*) OR ALL=(neutrophil*) OR ALL=(basophil*) OR ALL=(eosinophil*)) AND (ALL=(cognitive*) OR ALL=(attenti*) OR ALL=(vigilan*) OR ALL=(processing speed))
Psycinfo	Any Field: schizophrenia OR Any Field: schizophreniform OR Any Field: psychotic OR Any Field: psychosis OR Any Field: MDD OR Any Field: depressive disorder OR Any Field: major depression OR Any Field: manic OR Any Field: mania OR Any Field: bipolar OR Any Field: mood disorder OR Any Field: affective disorder OR Any Field: dysthymia AND Any Field: Immune OR cytokine OR chemokine OR interleukin OR CRP OR IL-1b OR IL-1β OR IL-1ra OR IL-2 OR IL-4 OR IL-6 OR IL-8 OR IL-10 OR IL-12 OR tumor necrosis factor OR TNF OR IFN OR IFN-γ OR Interferon OR kynurenine OR kynurenic OR quinolinic OR xanthurenic OR picolinic OR anthranilic OR HLA OR lymphocyte OR monocyte OR Leukocyte OR neutrophil OR basophil or eosinophil AND Any Field: cognition OR Any Field: executive functioning OR Any Field: reasoning OR Any Field: problem solving OR Any Field: memory OR Any Field: learning OR Any Field: processing speed AND Peer-Reviewed Journals only

Main outcome measure:

Correlation value (pearson's r or rho value) or regression coefficient (B value) reporting on the association between neuropsychological measure(s) (NP) and immune-related marker(s) (IM) will be included in the study.

The primary Immunomarker (IM) outcome variables will be two composite inflammatory indices

- Pro-inflammatory Index, PII
- Anti-Inflammatory Index, All

If only a single IM is included in the study, that IM x Neuropsychological measure correlation coefficient will be used for the PII/AII associations. If more IM are included, PII and AII will be calculated for each cognitive domain, averaging out the associations between that specific cognitive domain on one hand and the available immunomarker-based correlations on the other (based on Fisher's z transformation of the r values)."

Primary outcome of the study is PII/AII x composite score for all combined diagnoses. PII/AII x individual cognitive domains for combined diagnosis and the separate diagnoses (SZ, MDD, BD) will also be calculated and reported.

Additional outcomes

Secondary IM outcome variables are individual IM when >3 studies are available.

In case of a significant association, exploratory subgroup analyses will be performed to define which of the diagnoses contributes to the statistically significant association.

Data extraction:

Two reviewers (MM and CO) will independently evaluate the search results. Title and abstract of all search hits will be evaluated based on inclusion and exclusion criteria. Relevant or potentially relevant papers will be extracted:

- author, publication year, diagnosis, sample size, mean age, mean DOI, gender ratio, %smoking, mean BMI, name of cognitive domain, name of cognitive test, immune biomarker, tissue (serum, plasma, CSF, tracer, cells), bioanalytical method - correlation (pearson's r or rho value) or regression coefficient (B value) between neuropsychological measure(s) and immune-related biomarker(s), p-value.

- Number of neuropsychological tests included in the study

- number of immune biomarkers included in the study

- number of reported correlations

Data will be recorded in excel sheet.

Investigated cognitive domains and cognitive tests included

Domain	Tests			
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	Digit sequencing test, BACS-WM, MCCB-WM, delayed match			
	to sample test,			
Attention and vigilance	RBANS-attention, MCCB-attention, BACS-attention, CANTAB-			
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Processing speed	Digit Symbol Coding tests, TMTB			
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Risk of Bias Assessment:

Quality assessment of eligible papers was performed with the BIOCROSS evaluation tool, which is specifically developed for biomarker-based crosssectional studies

Strategy for meta-analysis

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- Correlation and 95% CI as well as Z-value and p value will be reported per study, as well as for the overall summary of the random model
- Analyses will be performed for:

- Composite cognitive score as well as individual cognitive domains
- Psychotic and mood disorders combined, as well as for three diagnostic groups separately (SZ, BD, MDD)
- For pro-inflammatory markers combined
- For anti-inflammatory markers combined
- For biomarkers that have been investigated in at least three different, independent studies in the same diagnosis (e.g. CRP, IL-6, IL-1b) for the same cognitive domain, separate meta-analyses will be performed