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**Affective Neuroscience Personality Scale (ANPS) and clinical implications:
A Systematic Review**

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All authors listed on the title page have read the manuscript and attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to online The Journal of Affective

ANPS AND CLINICAL IMPLICATIONS

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Author contributions

Lorenzo Brienza conceived the study and wrote the manuscript.

Alessandro Zennaro reviewed the manuscript.

Enrico Vitolo supervised the design review and reviewed the manuscript.

Agata Andò conceived the study, supervised the design review and wrote the manuscript.

ANPS AND CLINICAL IMPLICATIONS

Abstract

Background: Affective neuroscience (AN) theory assumes the existence of seven basic emotional systems (i.e., SEEKING, ANGER, FEAR, CARE, LUST, SADNESS, PLAY) that are common to all mammals and evolutionarily determined *to be tools* for survival and, in general, for fitness. Based on the AN approach, the Affective Neuroscience Personality Scales (ANPS) questionnaire was developed to examine individual differences in the defined basic emotional systems. The present systematic review aims to (a) examine the use of ANPS in clinical settings and (b) shed light on the utility of ANPS by identifying the personality structures that reflect endophenotypes predisposing to psychopathology.

Methods: The systematic review was conducted following the PRISMA statements. PubMed and PsycInfo were used for research literature from March 2003 to November 2021.

Results: Forty-four studies including ANPS were identified from 1763 studies reviewed. Sixteen studies met the inclusion criteria.

Limitations: The review comprised some papers with incomplete psychological assessments (e.g., lack of other measures in addition to the ANPS) and missing information (e.g., on the [sub]samples), which may affect the generalizability of findings.

Conclusion: Specific endophenotypes and/or patterns of emotional/motivational systems were found for several mental disorders. Specifically, endophenotypes emerged for Depressive and Autism Spectrum Disorders, Borderline and Avoidant Personality Disorders, type I and II Bipolar Disorders, and the Obsessive-Compulsive Disorder. The endophenotypes can provide useful elements of reflection for both psychodiagnostics and intervention. Overall, the current study represents the first contribution to understanding the basic emotional systems involved in psychopathological manifestations identified by AN.

Keywords: Affective Neuroscience, ANPS, Psychopathology, Systematic Review

Affective Neuroscience Personality Scale (ANPS) and clinical implications:

A Systematic Review

Introduction

The theory of Affective Neuroscience (AN), developed and elaborated by Jaak Panksepp (1991, 1992, 1998), is considered one of the most solid and established fields for the study of emotions at the psychological, neuroscientific, and psychiatric level. AN theory proposes seven phylogenetic and genetic primary emotional systems (i.e., SEEKING, ANGER, FEAR, CARE, LUST, SADNESS, PLAY) common to all mammals and localized in the ancient subcortical brain (Davis & Montag, 2019; Davis & Panksepp, 2018; Montag & Panksepp, 2017; Panksepp, 1998; Panksepp & Biven, 2012). Each basic emotional system has been evolutionarily shaped in terms of inherited tools for survival and, more generally, for fitness (Davis & Panksepp, 2018; Montag & Panksepp, 2017). Basic emotional systems can be unconditionally activated by evolutionarily selected triggers, but they can also act as *catalysts* (in terms of rewards or punishment) for memory and learning processes (Panksepp & Biven, 2012). The AN theory holds that these seven basic emotional systems consist of temperamental personality traits that control and influence an individual's behavior in the world (Montag, 2014; Montag & Reuter, 2014; Panksepp, 1998; Panksepp & Biven, 2012); moreover, the emotional systems could lead to dysfunctional expressions by generating excessive feelings, accompanied by extreme or distorted thoughts and behaviors. A key point is that the subcortical areas of the basic emotional systems are always able to overwhelm the regulatory and control functions of the most recent neocortex (Davis & Montag, 2019; Panksepp, 2011; Panksepp & Biven, 2012).

The development of the Affective Neuroscience Personality Scales (ANPS; Davis et al., 2003) is precisely based on the aforementioned assumptions. Emotional systems are components of motivational systems, which are psychological mechanisms that orient individuals toward biologically significant goals, organize behaviors, monitor them, and promote the learning of

ANPS AND CLINICAL IMPLICATIONS

strategies and skills (Del Giudice, 2018). The ANPS represents and describes the six primary emotional systems: *SEEKING*, *CARE*, *PLAY*, *FEAR*, *SADNESS*, and *ANGER*, and it is designed to measure them. We can note that the LUST scale was not in the ANPS because its inclusion might cause responding bias by compromising other ANPS item responses; in other words, it was deemed that investigating such an area of people's intimacy might reduce honesty in responding to items on the remaining scales. In addition, a scale named *Spirituality* has been added because of its general importance in human affairs, especially in addiction treatment programs (i.e., Alcoholics Anonymous) (Davis et al., 2003; Panksepp & Davis, 2018). The scales are divided into two superordinate factors: "General Positive Affect" and "General Negative Affect" (Davis et al., 2003). Basic positive emotions that constitute *General Positive Affect* include: the *PLAY* scale, defined as having fun, playing with physical contact, humor and laughter, and general enjoyment; the *SEEKING* scale, defined as anticipatory tendencies toward new positive experiences such as curiosity, seeking solutions to problems, and general joy of discovery; the *CARE* scale, considered as tendencies toward caring or behaviors such as concern for others, especially offspring, or general concern for persons or animals in need of help. Basic negative emotions that define *General Negative Affect* include: the *FEAR* scale, defined as feeling of anxiety, worry, rumination about past events, difficulty making decisions; the *SADNESS* scale, expressed by separation anxiety and loneliness, frequent crying, thoughts of past relationships and loved ones; the *ANGER* scale, characterized by irritability, frustration, and the expression of anger in verbal and physical forms. The *Spirituality* scale is related to a sense of being connected to creation as a whole (Davis et al., 2003; Davis & Panksepp, 2018).

According to the approach underlying the ANPS scales, each person *is born* with his or her own distinctive endophenotypes. Endophenotypes are invisible, measurable components that describe the pathway between a particular proximal phenotype and its distal genotype (Gottesman & Schield, 1972; Gottesman & Gould, 2003). An endophenotype (as well as basic emotional systems) includes neurophysiological, biochemical, endocrinological, neuroanatomical, or cognitive

ANPS AND CLINICAL IMPLICATIONS

and neuropsychological markers (Gottesman & McGue, 2015). The discovery of endophenotypes could be useful for knowledge and etiological understanding of mental suffering separating behavioral symptoms into more stable phenotypes with a clear genetic connection.

By studying endophenotypes, it is possible to understand the mechanisms of neuroanatomical and neurochemical circuitry, and pathways related to the interaction between genome and behaviors that underlie mental suffering (e.g., Gould & Gottesman, 2006; Iacono, 2018; Savitz & Drevets, 2009; Walters & Owen, 2007). There is evidence that ANPS scores can be used to assess emotional endophenotypes represented by basic emotional systems (Davis & Panksepp, 2018; Montag et al., 2011; Pingault et al., 2012; Panksepp, 2006), contributing to increase the knowledge of mental illness.

Aims

The aim of this systematic review is to (a) examine the use of ANPS in clinical setting and (b) shed light on the utility of ANPS by identifying the personality structures in the form of endophenotypes that are susceptible and predisposing to psychopathology (Panksepp, 2006).

Methods

Systematic review

The systematic review was conducted in accordance with the PRISMA-P statement and protocol (Shamseer et al., 2015).

Data source

Titles, abstracts, and topics were searched using the following terms: ((*mental disorder** OR *mental disease** OR *psychopatholog** OR *personality disorder**) AND *ANPS*) OR ((*mental disorder** OR *mental disease** OR *psychopatholog** OR *personality disorder**) AND *affective neuroscience personality scales*).

ANPS AND CLINICAL IMPLICATIONS

The electronic research literature databases included PubMed and PsycInfo. Data was searched during November 2021. Eligibility criteria were set to English language, sample with at least 18 years old and publication date from 2003¹ to 2021.

Study selection

The literature research was carried out by three investigators (A.A., L.B., E.V.); disagreements were resolved by consensus among these primary raters and the other investigator. Articles were eligible whether (1) subject were human, (2) the sample was at least 18 years old, (3) subjects had at least one psychiatric diagnosis according to the main diagnostic systems (DSM, ICD), and (4) studies were written in English. Studies in which participants did not have a formal psychiatric diagnosis (according to DSM, ICD) were excluded.

Data extraction

The following data was extracted from studies meeting the criteria for inclusion in the systematic review: other psychological measures besides ANPS, sample size, gender, age, mental disorder, study design, main findings, comorbidity, and diagnostic system.

Results

The literature search is summarized in Figure 1.

¹ Year of the first study that included ANPS as a tool.

ANPS AND CLINICAL IMPLICATIONS

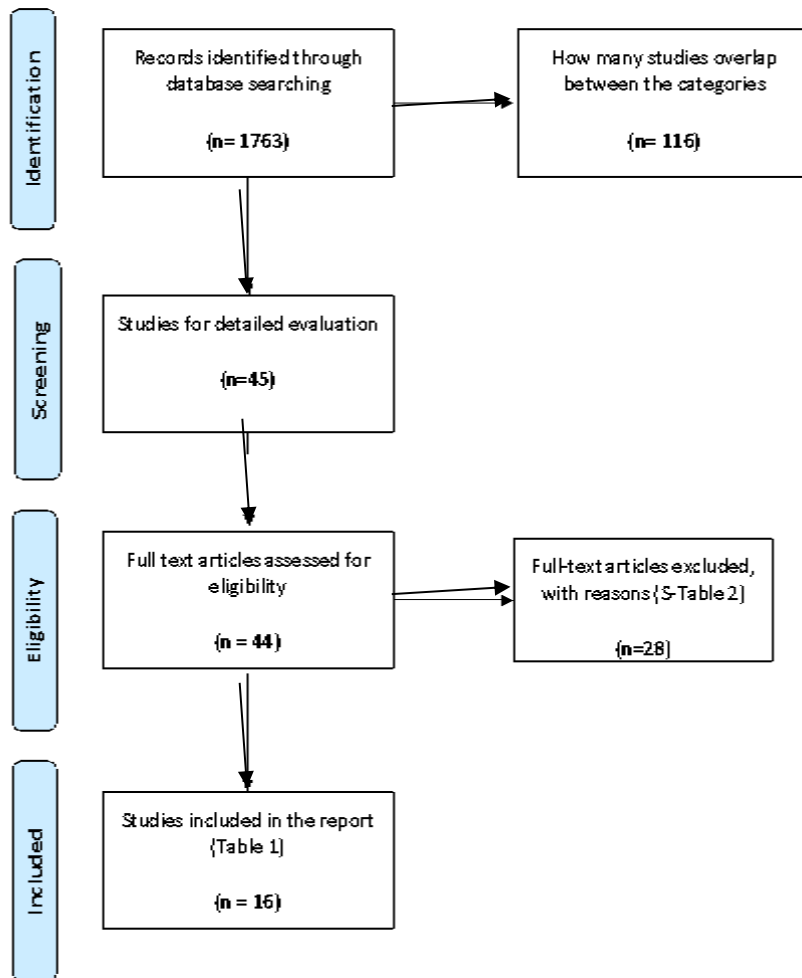


Figure 1. PRISMA Flow chart

Sixteen studies (Balchin et al., 2016; Carré et al., 2015; Fuchshuber et al., 2018; Fuchshuber et al., 2019; Giacolini et al., 2017; He et al., 2020; Jackson & Solms, 2014; Karterud et al., 2016; Lu et al., 2021; Montag et al., 2017; Pedersen et al., 2014; Sanwald et al., 2021; Savitz et al., 2008a, 2008b, 2008c; Unterrainer et al., 2017) met our inclusion criteria and were included in the present systematic review (See Table, 1; see also S-Table 2 for the list of excluded studies).

Please note that, for the purpose of our study, we decided to do not include the Spirituality scale in our dissertation for two reasons: firstly, because not all the ANPS (updated) versions include this scale (i.e., BANPS, ANPS-S); secondly, because our aim was to investigate which endophenotypes could be led to the etiology of the psychopathological phenomena that will be

ANPS AND CLINICAL IMPLICATIONS

discussed later, and the Spirituality scale is not associated with a specific endophenotype, as are the other ANPS scales.

ANPS AND CLINICAL IMPLICATIONS

Table 1.
Included studies

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
1. Balchin et al., 2016	Affective Neuroscience Personality Scales 2.4 (ANPS 2.4)	Total = 30	/	M = 25.4	Depression	Longitudinal	The decreased PANIC and FEAR across all groups, and the increased SEEKING suggesting that the PANIC system may be the mechanism underlying depression		Diagnosis based on MDI
	Major Depression Inventory (MDI)	High intensity exercise = 9							
	Hamilton Depression Rating Scale (HAM-D)	Moderate intensity exercise = 11							
	Montgomery-Åsberg Depression Rating Scale (MADRS)	Control = 10							

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
2. Carré et al., 2015	ANPS 2.4	Total = 40	Female = 30%	M = 26.3	Autism Spectrum Disorder	Cross-sectional	ASD is related to high levels of negative affectivity, and also to low levels of positive affectivity.		DSM-IV-TR
	Wechsler Adult Intelligence Scale, Third Edition (WAIS-III)	ASD = 20	Male = 70%	SD = 7.00			PLAYFULLNESS and FEAR were both related to ASD.		
	Revised Social Anhedonia Scale (SAS)	Healthy Control = 20					The effect size was medium for FEAR, and an increase of one point in the FEAR score corresponded to a 1.28-time increase in the likelihood of having an ASD diagnosis.		
	Autistic Socio-Affective Traits (AQ)						SEEKING despite a medium effect size		
	13-item Beck Depression Inventory (BDI-13)								

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
3. Fuchshuber et al., 2018	Autism Diagnostic Observational Schedule (ADOS-G)						difference between the ASD and the control group.		
	Affective Neuroscience Personality Scales (ANPS)	N = 500	Female = 63.2%	M = 26	Depression	Cross-sectional	No differences in SADNESS score.		
	The Childhood Trauma Questionnaire (CTQ)	Lifetime diagnosis = 187 (37.4%)	Male = 36.8%	SD = 5.51	Substance Use Disorder		The relationship of childhood trauma with primary emotions and personality organization are valid avenues to understanding the emergence of addiction and depression.		
	16-Item Inventory of Personality Organization (IPO-16)	Depression = 129							
	Brief Symptom Inventory-18 (BSI-18)	SUD = 9							
Alcohol, Smoking and Substance Involvement Screening Test (ASSIT)							Traumatic childhood experiences are associated with both disorders (depression and SUD). Restructuring of problematic dispositions toward SEEKING and SADNESS may be especially important		

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
							in the treatment of depression.		
4. Fuchshuber et al., 2019	ANPS Alcohol, Smoking, and Substance Involvement Screening Test (ASSIT) Brief Symptom Inventory (BSI-18)	N = 616 Lifetime diagnosis = 243 Depression = 147 Other affective disorders = 50 Other Psychiatric disorders = 46	Female = 61.9% Male = 38.1%	M = 30 SD = 9.53	Depression Substance Use Disorder	Cross-sectional	Interdependent relationship between primary emotions and personality organization, as well as a significant correlation between depression and addiction. Empirical evidence for the psychiatric significance of primary emotion dispositions. Specific pattern of primary emotion dispositions underlies symptoms of SUD and other psychiatric disorders.		
5. Giacolini et al., 2017	ANPS 2.4	Non clinical group = 625	Female = 41.28%	M = 30.41 %	Personality Disorder	Cross-sectional	Internal consistency was satisfactory and		DSM-5

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	The Big Five Inventory (BFI)	Clinical group = 218	Male = 58.72%	SD = 13.90	Substance Related and Addictive Disorder Depressive disorder Bipolar and Related Disorder Trauma and Stressor Related Disorder		the factor structures of the ANPS 2.4 was similar to the original version. ANPS scores and correlations were discussed in relation to individual differences, including psychiatric disorders.		

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
					Anxiety Disorder Schizophrenia Spectrum Disorder Feeding and Eating disorder				
6. He et al., 2020	ANPS Structured Clinical Interview for DSM-IV-TR-Patient Edition (SCID-P) Snaith-Hamilton Pleasure Scale (SHAPS)	N = 126 Depressed group = 63 Control group = 63	Female = 49.20% Male = 50.8%	M = 35.35 SD = 11.02	MDD	Cross-sectional	MDD show significant higher scores in FEAR, ANGER and SADNESS and significant lower scores in SEEKING and PLAYFULLNESS of traits characteristics as compared with healthy group.		DSM-IV-TR

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	Structural Clinical Interview for DSM-IV (SCID-II)						Reduced function connectivity between the left and the right amygdala, hippocampus could predict the SADNESS scores in MDD patients.		
	Hamilton Depression Rating Scale (HAMD-24)								
	Hamilton Anxiety Rating Scale (HAMA-14)								
	Magnetic resonance imaging (MRI)								
7. Jackson M. & Solms M., 2014	ANPS Meta-Cognitions Questionnaire (MCQ)	Study 1: N = 1119	Female = 73.12% Male = 26.88%	M = 33.4 SD = 9.685	Obsessive-Compulsive Disorder	Cross-sectional	Who score high on measures of obsessionality and low mood (as well as those with clinical OCD and MDD) exhibit significantly higher degrees of	OCD MDD	/

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	Padua Inventory (PI)	High obsessionality = 21			Major Depressive Disorder		separation distress, an inclination toward heightened activation of the PANIC system.		
	Major Depression Inventory (MDI)	Low obsessionality = 20					These studies establish that PANIC/separation distress is an important emotion system in obsessionality.		
	Positive and Negative Affect Scale (PANAS)	Study 2:							
	Separation Anxiety Symptom Inventory (SASI)	N = 49					A mediation analysis shows that these variables (OCD, MDD and PANIC) are strongly and significantly linked via a generative mechanism.		
	Structured Clinical Interview for Separation Anxiety Symptoms (SCI- SAS)	Highest scoring (combined measures of obsessionality and low mood) = 25							
	Adult Separation Anxiety Checklist (ASA-CL27)	Lowest scoring (combined measures of							

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	Tale-Brown Obsessive-Compulsive Scale (Y-BOCS)	obsessionality and low mood) = 24 Study 3 (clinical): Clinical group (OCD and/or MDD) = 84 Control group = 75					Separation trauma in early childhood was highly associated with whether the participants were diagnosed with OCD and/or MDD; that incidence could prove useful as a predictive factor in the adult development of these disorders. Separation distress mediates the relationship between OCD and MDD.		
8. Karterud et al., 2016	ANPS 2.4 Brief Affective Neuroscience Personality Scales (BANPS)	Total = 546 Schizoid = 1 Schizotypal = 6 Paranoid = 45	Female = 77% Male = 23%	M = 32 SD = 8	Personality Disorder	Cross-sectional	A range of significant associations occur between the criteria of PDs and the ANPS. Unique contribution of each primary		DSM-IV

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	Short Version of the Affective Neuroscience Personality (ANPS-S)	Borderline = 210 Antisocial = 4 Narcissistic = 18 Histrionic = 3 <i>Digitare l'equaz</i> Avoidant = 150 Dependent = 26 Obsessive-compulsive = 39 PD NOS = 104					emotions to the different PDs. The model explain 19% of the variance in borderline and avoidant PD.		
9. Lu et al., 2021	ANPS 2.4	No PD = 89 Total = 106 BDD = 43	Female = 48.1%	M = 33.06 SD = 10.5	BDD	Cross-sectional	BDD patients showed / significant higher negative and lower		DSM-IV-TR

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	Structured Clinical Interview for DSM-IV-TR-Patient Edition (SCID-P)	Control = 63	Male = 51.9%				positive emotional endophenotypes of ANPS than Healthy control participants (HC).		
	Structured Clinical Interview for DSM-IV-Non-Patient Edition								
	Hamilton Depression Rating Scale (HAM-D-24)						The results yielded altered FC patterns in the prefrontal-limbic-striatum system; those patterns yielded 84.91% accuracy with 93.65% sensitivity and 72.09% specificity in distinguishing BDD patients from HCs.		
	Hamilton Anxiety Rating Scale (HAM-A-14)								
	MRI						The decreased FC of right OFC-right PUT/CAU was positively correlated with SADNESS and FEAR scores. FEAR scores were positively associated with reduced FC of left PUT-right OFC		

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
10. Montag et al., 2017	ANPS Beck's Depression Inventory-II (BDI-II) Structured Clinical Interview for DSM-IV (SCID)	Non-clinical group = 625 Depressed patient = 55	Female NC = 71,68% Male NC = 28.32% Female D = 63,63% Male D = 36,37%	M NC = 23.54 SD NC = 5.91 M D = 42.44 SD D= 13.68	Depression	Cross-sectional	decreased FC of right MFG-right insula. The negative emotional endophenotypes associated with disrupted prefrontal- limbic-striatum connection might be a neurobiological underpinning and biomarker for BDD. Robust associations appeared between higher FEAR and SADNESS scores and depressive tendencies. A weaker association was observed with lower SEEKING scores and higher depressive tendencies.		DSM-IV

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
11. Pedersen et al., 2014	ANPS 2.4 BANPS ANPS-S	Total = 546 Schizoid = 1 Schizotypal = 6 Paranoid = 45 Borderline = 210 Antisocial = 4 Narcissistic = 18 Histrionic = 3 Avoidant = 150 Dependent = 26 Obsessive-compulsive = 39 PD NOS = 104 NoPD = 89	Female = 77% Male = 23%	M = 32 SD = 8	Personality Disorder	Cross-sectional	Full ANPS revealed acceptable internal consistencies. Factor analyses revealed poor fit for a six factor solution. High correlations between PLAY and SEEK, and between SADNESS and FEAR. Better psychometric properties in the two short version (BANPS and ANPS-S)		DSM-IV

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
12. Sanwald et al., 2021	ANPS	N = 146	Female = 65.1%	M = 38.74	MDD	Cross-sectional	Young age at depression onset is associated with depressive symptom severity. A considerable amount of variance in depression onset can be explained by sex, the experience of stressful life events and high SADNESS and low SEEKING ANPS's scores.	Alcohol abuse Sexual dysfunction not otherwise specified	DSM-IV
	Structured Clinical Interview for DSM-IV (SCID-I)		Male = 34.9%	SD = 14.25					
	Montgomery-Åsberg Depression Rating Scale (MADRS)								
	Standardized semi-structured interview based on an in-house questionnaire								
	Critical Life Events Questionnaire (CLEQ)								
	BDI-II								
13. Savitz, van der Merwe, & Ramesar, 2008	ANPS	N = 300	Female = 55%		Bipolar Disorder I	Longitudinal	Depressive temperament scores as measured by the DT and the SADNESS scales, were highest in the BPD groups. Anxious temperament traits as	Alcoholism GAD Dysthymia Phobia Schizophrenia	DSM-IV
	The Temperament and Character Inventory (TCI-240)	Control = 88 BPD I = 58	Male = 45%		Bipolar Disorder II				
	The Temperament Evaluation of Memphis (TEMPS-A)	BPD II = 27 MDE-R = 58			Major Depressive Episode Single				

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	The Beck Depression Inventory (BDI)	MDE-S = 45			Major Depressive Episode Recurring		measured by the FEAR subscale of the ANPS did not lead to significant differences between the groups	ADHD	()
	The Altman Sel-Rating Mania Scale (ASRM)	Other = 24						Borderline PD Cyclothymia Delusional Disorder DNOS Deferred	
14. Savitz, van der Merwe, & Ramesar, 2008	ANPS	N = 296			57 BPD I	Cross-sectional	ANGER (a measure of cyclothymic and hostile traits with TEMPS-A CT and IT) is higher in BPD I, BPD II and MDE-R groups.	Alcoholism	DSM-IV
	The Temperament and Character Inventory (TCI-240)	BPD I = 57			24 BPD II			GAD	
		BPD II = 24			58 MDE-R			Dysthymia	
	The Hypomanic Personality Questionnaire (HPS)	MDE-R = 24			45 MDE-S		The SEEKING and PLAYFULLNESS scales did not differentiate the diagnostic group.	Phobia	
		MDE-S = 45						Schizophrenia	

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
	The Temperament Evaluation of Memphis (TEMPS-A)	Unaffected = 86			7 Alcohol related			ADHD	
	The Borderline Traits Questionnaire (STB)				1 Cyclothymia			Borderline PD	
	The Beck Depression Inventory (BDI)				3 Dysthymia			Cyclothymia	
	The Altman Self-Rating Mania Scale (ASRM)				2 Schizophrenia			Delusional disorder	
					4 GAD			DNOS	
					1 ADHD			Deferred	
					1 Delusional Disorder				
					25				

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
15. Savitz, van der Merwe, & Ramesar, (2008)	ANPS Structured Clinical Interview (SCID) Beck Depression Inventory (BDI) Altman Self-Rating Mania Scale (ASRM) Temperament and Character Inventory (TCI)	N = 241 BD I = 55 BD II = 20 MDE-R = 48 MDE-S = 30 Unaffected = 67	Female = 57.3% Male = 42.7 %	M = 48.43 SD = 16.63	4 DNOS 1 Borderline Personality Disorder 2 Phobia 86 unaffected Bipolar Disorder I Bipolar Disorder II Major Depression	Longitudinal	The 10R VNTR allele of the SLC6A3 gene was significantly associated with lower self-directedness		DSM-IV

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
16. Unterrainer, Hiebler-Ragger, & Krioschuntnig, 2017	The Hypomanic Personality Questionnaire (HPS)								
	The Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Auto questionnaire (TEMPS-A)								
	Adult Attachment Scale (AAS)	N = 59	/	M = 23.95	Poly-drug use disorder (PUD)	Cross-sectional	PUD patients exhibited higher levels of ANGER, FEAR and SADNESS.		ICD 10
	Multidimensional Inventory for Religious/Spiritual Well-Being (MI-RSWB)	PUD = 20		SD = 1.91			No differences in SEEKING, CARE or PLAYFULLNESS.		
	Wonderlic Personnel Test (WPT)	RUC (nicotine) = 20					SADNESS or FEAR tend to be related to impaired white matter.		
	MRI	NUC = 20							

ANPS AND CLINICAL IMPLICATIONS

Study	Psychological measures	Sample	Gender	Age (mean/SD)	Mental Disorder	Study Design	Main findings	Comorbidity	Diagnostic System
							It was not observing a decreased existential well-being in PUD patients.		
							No differences in parameters of spirituality between PUD and control groups.		

Note: ADHD: Attention Deficit Hyperactivity Disorder; APD: Avoidant Personality Disorder; ASD: Autism Spectrum Disorder; ASPD: Antisocial Personality Disorder; BD-I: Bipolar I Disorder; BD-II: Bipolar II Disorder; BPD: Borderline Personality Disorder; DNOS: Not Otherwise Specified Disorder; GAD: General Anxiety Disorder; HPD: Histrionic Personality Disorder; MDD: Major Depressive Disorder; MDE-R: Major Depressive Recurrent Episode; MDE-S: Major Depressive Single Episode; NPD: Narcissistic Personality Disorder; OCD: Obsessive-Compulsive Disorder; OCPD: Obsessive Compulsive Personality Disorder; PD: Personality Disorder; PPD: Paranoid Personality Disorder; PUD: Poly-drug Use Disorder; RUC: Recreational-Drug Use; SPD: Schizotypal Personality Disorder; SUD: Substance Use Disorder.

ANPS AND CLINICAL IMPLICATIONS

Discussion

Overall findings

By reviewing researches that used ANPS in clinical settings, we can better understand the different emotional patterns involved in the endophenotypes that characterize the wide variety of symptom expression in each nosographic category. The studies reviewed and included allow us to conduct a preliminary analysis of the current state of the art of ANPS in clinical settings. To this end, the organization of this section follows a structure based on psychopathological clusters and labels, based on the admission criteria we established, according to which a prior diagnosis based on the main diagnostic system (i.e., DSM, ICD) was required. This categorization allows us to observe how the tool is articulated and, consequently, to draw conclusions about its use in the clinical setting. Moreover, for each section, we present the main emotional endophenotypes that characterize each psychopathological manifestation, according to what emerged.

The results were listed and described below in order of DSM-5 classification (e.g., Neurodevelopmental Disorders, Schizophrenia Spectrum and Other Psychotic Disorders).

Autism Spectrum Disorder: low PLAY and high FEAR

From the perspective of AN theory, three basic emotional systems are primarily involved in the disorders underlying the development and exchange of deficits in social reciprocity: the CARE, SADNESS, and PLAY systems (Panksepp, 1998; Sivy & Panksepp, 2011; Waterhose, 2012). In addition, Panksepp et al. (1991) examined the role of elevated endogenous opioids levels as a cause or concomitant of impairments in social attachment symptoms in Autism Spectrum Disorders (ASD; American Psychiatric Association, 2013). Carré et al. (2015) administered the French adaptation of ANPS - version 2.4 (Pahlavan et al., 2008; Pingault et al., 2012) - in a sample of 20 participants with ASD compared to a control group with similar age, IQ and educational level. Results outlined significant differences for each scale but, contrary to expectation, no significant differences on the SADNESS scale were found. The largest difference between groups was found on the PLAY scale (Carré et al., 2015). Through a logistic regression, in which all scales of the

ANPS AND CLINICAL IMPLICATIONS

ANPS were included, the PLAY and the FEAR scales were the only significantly predictive scales for the diagnosis of ASD. In addition, separate measures of autistic traits were strongly related to lower PLAY scores, which could be representative of social bonding impairments that characterize the ASD (Carré et al., 2015). Regarding the FEAR scale, the authors argued how it might be linked to a sort of tension and worry feelings due to changes in the environmental, relational, and social context (Carré et al., 2015). Further, fear manifestation could lead to an increased need for “sameness” (e.g., Gotham et al., 2013; Rodgers et al., 2012). Notably, the PLAY scale appeared to be the only significant predictor of autistic traits. The last point can be further explored by considering that the PLAY scale of the ANPS correlates positively with the Extraversion trait of the Big Five (Davis et al., 2003; for a meta-analysis of correlations between ANPS and Big Five, see Marengo et al., 2021). Indeed, autism-like traits show a correlation with low levels of Extraversion (Austin, 2005; Schwartzman et al., 2016). Wakabayashi et al. (2006) found that the trait Extraversion correlated negatively with the Autism Spectrum Quotient (AQ), particularly with the subscales Social Skills, Imagination, Attention Shift, and Communication, which may represent other core components of the PLAYFULNESS dimension (Davis et al., 2003; Panksepp, 1998). Indeed, Davis and colleagues (2003) have argued that the PLAY system could be conceptualized as the root of the trait extraversion, which first appears in childhood in the form of smiling, laughing, and sensitivity to tickling and later develops in adulthood in the form of social fun and interactions. The aforementioned findings may bridge low Extraversion, low AQ scores, and low PLAY in individuals with autistic-like traits. This is another reason why the PLAY scale seems to be the strongest predictor of autistic-like traits. The findings support the shared idea that social bonding deficits may be strong predictors for the identification and diagnosis of ASD (e.g., Aikten, 2008; Baron-Cohen et al., 1992; Jordan, 2003).

Bipolar Disorders: high SADNESS

With respect to bipolar disorders, there are four studies that have used ANPS (Lu et al., 2021; Savitz et al., 2008a, 2008b, 2008c), and they are summarized in the following section. Savitz

ANPS AND CLINICAL IMPLICATIONS

et al. (2008a, 2008b, 2008c) conducted studies in which ANPS was administered to a sample of individuals with Bipolar Disorder I (BD-I; American Psychiatric Association, 2013) and Bipolar Disorder II (BD-II; American Psychiatric Association, 2013) compared to individuals with Major Depressive Episode Recurrent (MDE-R), Major Depressive Episode Single (MDE-S), and individuals without any psychiatric diagnosis. All of these groups were from a sample of families with bipolar disorder (BD). In the first study, only the SADNESS and FEAR scales were used to assess the subjects' depressed and anxious feelings, respectively. The BD-I group scored high on both scales, but they were the only ones who scored significantly high on SADNESS scale compared to the other groups (Savitz et al., 2008a). In another study, Savitz et al. (2008b) included the ANPS to test hypomanic and cyclothymic hostile personality traits. Specifically, the authors argued that the SEEKING scale could attest to hypomanic personality traits, whereas the high ANGER scale could support cyclothymic-hostile personality traits. Scores for the SEEKING and PLAY scales did not differ between diagnostic groups. Significantly higher ANGER scores were found in the BD-II group (Savitz et al., 2008b). Finally, Savitz et al. (2008c) examined several different variants of candidate genes associated with BD. Unfortunately, no significant associations with ANPS were found (Savitz et al., 2008c). More recently, Lu et al. (2021) investigated the relationship between functional connectivity (FC) of the prefrontal-limbic-subcortical network and emotional endophenotypes in subjects with BD during depressive episodes (BDD) by comparing them with healthy controls (HC). They found that FC alterations were associated with emotional endophenotypes in BDD patients. Specifically, BDD patients, compared to HCs, showed significant decreases in positive affectivity on the PLAY and SEEKING scales and significant increases in negative affectivity on the FEAR, ANGER, and SADNESS scales (Lu et al., 2021). No differences were found between groups on the CARE scores. Moreover, the SADNESS and FEAR dimensions correlated positively with decreased FC between the right orbital frontal cortex (OFC) and the right putamen (PUT)/caudate (CAU) nucleus. In addition, FEAR was also positively related to decreased FC between the left PUT and right OFC and decreased FC between the right middle frontal gyrus

ANPS AND CLINICAL IMPLICATIONS

(MFG) and right insula (Lu et al., 2021). It is well known that the prefrontal-limbic-subcortical network plays a key role in integrating emotional information and regulating the intensity of emotional responses (Fuster, 2001), and the abnormal FC of the PFC network and limbic system leads to emotional dysregulation in depressed patients (Graham et al., 2013; Ochsner et al., 2012). In summary, BDD patients scored higher on the FEAR, ANGER, and SADNESS scales and lower on the SEEKING and PLAY scales, and these emotional endophenotypes were connected to a disrupted prefrontal-limbic-subcortical network (Lu et al., 2021). In addition, ANPS scales can contribute to a better characterization of the different psychopathological profiles between BD-I and BD-II patients.

Depressive Disorders: low SEEKING, PLAY and high SADNESS, FEAR, ANGER

Strong activation of the SADNESS system (hence, a state of negative emotionality) and a low activity of the SEEKING system (hence, less energy and motivation) is, in respect of the AN theory, the main characteristic of depressive disorders (Panksepp & Watt, 2011). This perspective to depressive etiology is also in agreement with an evolutionary perspective (Watt & Panksepp, 2009).

Based on AN theory, it is expected that individuals with depressive disorders will have low scores on SEEKING scale and high scores on SADNESS scale. In addition, it is useful to remember that high activation of the FEAR system (hence, high scores on the FEAR scale of the ANPS) can be observed, as anxious symptoms are strongly associated with depressive symptoms (e.g., Choi et al., 2020). The study conducted by Montag et al. (2017) implemented the ANPS to investigate individual differences among depressive subjects. The authors found low SEEKING scores, and high FEAR and SADNESS scores in depressed patients (Montag et al., 2017). In addition, low scores have been observed on the PLAY dimension. Regarding the latter finding, the authors argued how the high PLAY activity can be achieved if the *living environment* is perceived as safe and socially stimulating, which is not the case in depressed patients. The latter argument is also supported by the high FEAR scores, which are related to anxiety states/characteristics, which in

ANPS AND CLINICAL IMPLICATIONS

turn are related to the living environment (Montag et al., 2017; Panksepp & Biven, 2012). Similar findings were also reported by He et al. (2020), who administered the ANPS to a sample of sixty-three patients diagnosed with Major Depressive Disorder (MDD; American Psychiatric Association, 2013) compared to a non-clinical population. As expected, MDD patients reported significantly lower SEEKING and PLAY scores, and significantly higher FEAR, ANGER and SADNESS scores (He et al., 2020) when compared to healthy subjects. Noteworthy, as observed by Montag et al., 2017, increased the ANGER scores seemed to be due to an overlap between the FEAR and SADNESS scales. Moreover, in line with previous studies (e.g., Deris et al., 2017), the authors found how reduced FC between the amygdala and the bilateral hippocampus might be predicted by SADNESS scores in MDD patients (He et al., 2020). To explain the amount of variance of each ANPS scales in the scores related to the Beck Depression Inventory II, the authors formulated a hierarchical regression model. The model failed in finding a role of the ANGER dimension in explaining variance in subjects diagnosed with depression. However, it has been outlined how the dimension that tends to explain the most variance was the SADNESS scale (17.3%). The aforementioned findings were further supported by Balchin et al. (2016), which administered the ANPS to a sample of depressed individuals. In addition, the authors administered different intensities of physical exercise to three groups of depressed patients divided by different exercise intensity (low, medium, and high intensity) with the aim of improving depressive symptoms through the release of β -endorphins. The rationale was that the body produces β -endorphins to help with mental pain (a feeling characterized by the activation of the SADNESS system, which is built on the same pathways of the pain system) (e.g., Peter et al., 1990). The release of β -endorphins could lead to an improvement in depressive symptoms, and several studies have highlighted how physical exercise, which could increase the production of β -endorphins (Dishman and O'Connor, 2009), might be beneficial for depression (Dinas et al., 2011; Schuch et al., 2018). The authors hypothesized that exercise (hence, the release of β -endorphins) results in an analgesic effect on the SADNESS system with a consequent improvement in depressive symptomatology. The authors

ANPS AND CLINICAL IMPLICATIONS

verified this hypothesis throughout the use of ANPS and the values of β -endorphins measured weekly (Balchin et al., 2016). Fuchsuber et al. (2019) used the ANPS in a mixed population of depressive, anxious, somatization, and substance addiction patients, obtaining results in line with Montag et al. (2017). Moreover, the authors identified in the SADNESS scale the best predictor of depression, with further positive associations between depressive tendencies and ANGER and FEAR systems, and negative associations with PLAY and SEEKING systems. Finally, the authors investigated the relationship between childhood trauma, depressive symptoms, and primary emotional systems, highlighting a strong link between the SADNESS dimension and childhood trauma (Fuchsuber et al., 2019). Sanwald et al. (2021) found how the age of depression onset was positively associated with stressful life events (SLE), SADNESS scale, and severity of depressive symptomatology. By contrast, the age of depression onset was negatively associated with the SEEKING scale. Specifically, through a stepwise regression analysis, it was observed how the SADNESS scale was associated with a lower age of depression onset, sharing a certain amount of variance explained by SLEs, the SEEKING scale and gender, while high scores on the SEEKING scale were associated with a higher age depression onset.

Based on these findings, we may assert that subjects with depressive symptoms are characterized by high SADNESS, FEAR, and ANGER values and low PLAY and SEEKING values, thus being consistent with the predictions of AN theory (e.g., Panksepp & Watt, 2011). From a clinical perspective, these findings could shed fruitful light on atypical depressive manifestations, whose symptom constellation, collectively described as "reversed vegetative symptoms" (Parker et al., 2002), namely hyperphagia and hypersomnia, could be understood in terms of a different relationship between emotional systems (Juruena et al., 2018).

Obsessive-Compulsive Disorder (and related disorders): high SADNESS

Regarding the Obsessive-Compulsive Disorder (OCD; American Psychiatric Association, 2013), only Jackson and Solms (2014) used the ANPS to examine the role of the SADNESS scale in individuals with OCD and MDD. Results showed a significant positive correlation between high

ANPS AND CLINICAL IMPLICATIONS

SADNESS scores and diagnosis of OCD and MDD (Jackson & Solms, 2014). The authors hypothesized that obsessive-compulsive symptomatology may represent the active phase of separation distress, in which the person responds to the strong sense of loss, whereas depression may represent the despair phase of the separation response. Furthermore, the authors suggest that obsessive-compulsive, depressed, and panic disorder exist on a spectrum based on disruption of the circuitry of the SADNESS system (Jackson & Solms, 2014).

Substance Use Disorders and Addiction Disorder: high SADNESS

Three studies addressed the relationship between ANPS and Substance-Related and Addictive Disorders (Fuchsuber et al., 2018; Fuchshuber et al., 2019; Unterrainer et al., 2017). Unterrainer et al. (2017) used the BANPS (Barrett et al., 2013) in subjects with multiple substance use disorder (Poly-Drug Use, PUD), a group of tobacco smokers (Recreational-Drug Use, RUC), and a group of subjects who were non-smokers and reported never having used illicit substances (Non-Drug Users, NUC). The PUD group reported positive correlation with the ANGER, FEAR and SADNESS scales compared to the other two groups, whereas no significant differences were observed on the SEEKING, CARE and PLAY scales. Furthermore, controlling for the RUC group, only the PUD group showed a positive correlation for SADNESS and FEAR scales compared to general population (Unterrainer et al., 2017). As expected, SUD group showed heightened SEEKING scores, probably due to the symptomatic manifestation typical of SUD, such as the craving phenomenon, or the intense activation of the reward system (APA, 2013). Moreover, the AN theory considers the SEEKING system as hyper-activated in individuals with SUD (e.g., Alcaro & Panksepp, 2011; Weight & Panksepp, 2012), thus giving further support to these findings. Contrary to expectations, no positive correlation was found with the SEEKING scale. It could be possible that the high SADNESS score in the PUD population might physiologically de-activate the SEEKING system, thus leading to the results described above. The results by Unterrainer et al. (2017) were also supported by Fuchshuber et al. (2018, 2019), which found a predominant role SADNESS and ANGER dimensions in a SUD sample. The authors emphasized the role of

ANPS AND CLINICAL IMPLICATIONS

addiction as an attachment disorder, directly related to dysregulation within the endogenous opioid system (Burkett & Young, 2012; Flores, 2004; Fuchshuber et al., 2019; Montero González & Mondragòn, 2016).

Personality Disorders

Karterud et al. (2016) aimed to investigate whether the ANPS scales have sufficiently good properties to capturing different patterns of emotional endophenotypes within a PDs population. Although the sample was relatively large ($n = 546$), the most frequent PDs were Borderline Personality Disorder (BPD) (38,5%) and Avoidant Personality Disorder (APD) (27,5%). Through a series of regression analyses, the authors have found how ANPS explained 19% of the variance of BPD and APD, while tending to explain less variance for the other PDs (from 3-10%). Furthermore, the BANPS (Barrett et al., 2013) explained 20% of the variance for BPD, and 16% for the APD (Karterud et al., 2016).

BPD was defined by a strong positive correlation with ANGER, SADNESS, PLAY, and SEEKING scales (Karterud et al., 2016). As expected, APD showed strong positive correlations with the FEAR dimension (e.g., Denny et al., 2015), and negative correlations with the PLAY and SEEKING dimensions (Karterud et al., 2016). These results are particularly interesting when considering Panksepp's theories of activation and deactivation of various basic emotional systems (Panksepp, 1998; Panksepp & Biven, 2012). In particular, the AN theory postulates that different basic emotional systems are able to enhance or inhibit each other's activity (Panksepp, 1998; Panksepp & Biven, 2012). This type of "play" has even been found in psychiatric manifestations such as depression, where elevated levels of SADNESS are associated with low levels of SEEKING, characterizing the major depressive endophenotype (Panksepp & Watt, 2011). Consistent with these considerations, Karterud and colleagues (2016) argued how sustained activation of the FEAR system tends to inhibit that of the PLAY (and thus social bonding) and SEEKING systems, and outlined how activation and deactivation systems can occur even in APD patients. The last two associations tend to explain the interplay between interconnections that

ANPS AND CLINICAL IMPLICATIONS

occurs between activation and de-activation across different basic emotional systems. Keep in mind how Panksepp (1998; Panksepp & Biven, 2012) detailed how different basic emotional systems are able to enhancing or inhibiting each other's activity (Panksepp, 1998; Panksepp & Biven, 2012), this is particularly evident in Panksepp and Watt's (2011) theory in relation to depression. Specifically, the strong tendency for persistent activation of the FEAR system would tend to inhibit those of the PLAY (hence, social bonding) and SEEKING systems (Karterud et al., 2016).

Regarding the Schizoid Personality Disorder, a negative association with the CARE system was observed, thus confirming the restricted affectivity and the social detachment that characterize this PD (Karterud et al., 2016). Schizotypal Personality Disorder (SPD) has shown a negative correlation with PLAY and CARE scales (Karterud et al., 2016), which may be due to impairment and severe discomfort in social relationship and problems in dealing with intimacy (Dickey et al., 2005; Morken et al., 2014). Paranoid Personality Disorder (PPD) is defined by marked hostility (Falckum et al., 2009). Consequently, the strong positive correlation with ANGER scale and the negative correlation with the CARE scale is not surprising (Karterud et al., 2016); in addition, PPD showed also a positive correlation with the SADNESS scale (Karterud et al., 2016), which could be linked to experience of childhood trauma and social stress (Lee, 2017).

Given that fearless is one of the main components of Antisocial Personality Disorder (ASPD) (Cardinale et al., 2021; Vitale & Newman, 2008), findings regarding a negative association between the FEAR scale and ASPD was not surprising (Karterud et al., 2016). Moreover, the authors outlined a positive correlation with the ANGER scale and a negative correlation with the CARE scale (Karterud et al., 2016), which were probably due to the callous-unemotional component of ASPD (Allen et al., 2018).

Narcissistic Personality Disorder has shown a positive correlation with the SEEKING scale (Karterud et al., 2016), which tend to express the typical extraversion trait of these patients, particularly the grandiose type (Campbell & Miller, 2011; Zajenkowski & Szymaniak, 2019). In addition, negative correlations with CARE scale and positive inclination to the ANGER scale were

ANPS AND CLINICAL IMPLICATIONS

observed (Karterud et al., 2016), likely reflecting the tendency for low emotional empathy in these individuals (Ritter et al., 2011).

Histrionic Personality Disorder was associated with high SADNESS and PLAY scores (Karterud et al., 2016). Particularly regarding the latter dimension, the authors outlined how it may be related to the impressionistic speech style and theatrical emotional expression components that characterize these individuals (American Psychiatric Association, 2013).

Dependent Personality Disorder is characterized by intense feelings due to separation anxiety, and showed a strong disposition to high scores on the SADNESS dimension (along with BPD). In addition, given the strong structural anxiety dimension characterizing this PD (APA, 2013), high scores on the FEAR scale were not surprising (Karterud et al., 2016).

Obsessive Compulsive Personality Disorder (OCPD) expressed a high positive correlation with the ANGER and SEEKING dimensions, and a negative correlation with the PLAY scale, which could be explained with the typical rigidity of these patients (Karterud et al., 2016). In the same study, the authors collected some predictions related to the use of ANPS, thanks to the collaboration of five psychiatrists, who worked in the assessment and PDs treatment fields, and were familiar with AN theory. Specifically, the professionals were asked to predict the positive, negative, or absent associations between different prototypes of PDs and ANPS scales. When three or more clinicians agreed on the associations, they were considered valid for prediction verification (Karterud et al., 2016). Clinicians had difficulty dealing with the SEEKING dimension, probably because of the insufficient emphasis in psychotherapy with respect to behaviors characterizing the primary emotion SEEKING (Karterud et al., 2016).

Additional Clarifications

Giacolini et al. (2017) conducted a reliability and validity study of the Italian version of the ANPS 2.4 with both clinical (218 psychiatric patients) and non-clinical samples (625 healthy subjects). Their results showed differences between the clinical and nonclinical samples in terms of PLAY, SEEKING, CARE, and, in general, the superordinate factor "general positive affect," for

ANPS AND CLINICAL IMPLICATIONS

which the clinical sample reported significantly lower scores compared with the nonclinical sample. In addition, a slight difference was found between the groups with respect to the ANGER system, for which the non-clinical sample scored significantly lower than the clinical sample. Furthermore, the PLAY scale was found to be negatively related to the FEAR and SADNESS scales in the clinical sample. Finally, the SEEKING scale was positively correlated to the FEAR scale scores (Giacolini et al., 2017). The authors also examined gender differences in the clinical sample, founding significantly higher scores in women on FEAR, ANGER, and SADNESS dimensions (for gender differences in the ANPS, see also Abella et al., 2011; Davis et al., 2003; Davis & Panksepp, 2011; Montag et al., 2016; Montag & Panksepp, 2017; Orri et al., 2016; Orri et al., 2017; Oezakar-Gradwohl et al., 2014; Oezakar-Gradwohl et al., 2019; Pahlavan et al., 2008). Pedersen et al. (2014) conducted a study on a clinical sample characterized by PDs. They compared different versions of the ANPS (ANPS 2.4, ANPS-S, and BANPS), confirming the previous results by Giacolini et al. (2017). The intent in reporting these two studies is to get the reader able to evaluate and compare the different versions of the ANPS in studies including clinical populations. In addition, these studies allow us to highlight an observable trend in clinical psychopathology settings. The clinical population presents significantly lower scores on the scales of General Positive Affect, i.e., SEEKING, PLAY, and CARE. This finding could be interpreted in light of the fact that the basic emotional systems are interdependent. Indeed, activation of a particular system may lead to activation and/or de-activation of another system (e.g., sustained activation of the SADNESS system is accompanied by systematic de-activation of the SEEKING system) (Panksepp, 1998; Panksepp & Biven, 2012).

Conclusion

The aim of the present work was to investigate what knowledge can be gained from the application of the ANPS in the clinical setting. Based on the literature review, we identified some patterns of the emotional systems that characterize the psychopathological phenomena described above. In relation to depressive symptomatology and MDD (the most common

ANPS AND CLINICAL IMPLICATIONS

psychiatric manifestation), we observed a pattern characterized by high SADNESS, FEAR, and ANGER scores and low PLAY and SEEKING scores. The SADNESS scale appeared to be the most informative dimension for depressive disorders and was found to be positively related not only to MDD but also to OCD. ASD seem to be described by high FEAR scores and, more importantly, by low PLAY scores, which seems to be the most important predictor for this disorder. BPD is characterized by high scores on ANGER, SADNESS, and SEEKING scales, and APD by high scores on the ANGER, FEAR, and CARE scales. Each manifestation associated with SUD appears to be characterized by a high SADNESS dimension. Contrary to the assumption of the AN theory, no positive association was found between SUDs and the SEEKING dimension. BD-I was associated with the SADNESS scale, whereas the ANGER dimension was positively associated with BD-II. In addition, individuals with BD during depressive episodes showed significantly decreased scores for positive affectivity on the PLAY and SEEKING scales and significantly increased scores for negative affectivity on the FEAR, ANGER, and SADNESS scales. Finally, individuals with a psychiatric diagnosis and non-clinical individuals were found to be different by negative associations on the higher-level dimension of "General Positive Affect" (namely, on the scales SEEKING, CARE, and PLAY).

Conceptualizing psychopathological manifestations as results of imbalanced emotional systems activity, such as assumed in AN theory (Davis & Panksepp, 2018), could have significant implications for clinical approaches. Indeed, it could be plausible establishing a link between specific psychopathological manifestations and their emotional endophenotypes, which could be represented by the emotional-affective subcortical circuits identified by the ANPS (Panksepp, 2006). In this way, the primary emotional systems may assume the status of a motivational basis of personality. Indeed, thanks to their investigation, it might be possible to identify and formulate a nosographic diagnosis based on neuroscientific findings (Giacolini et al., 2017).

Moreover, since the primary emotional systems constitute the emotional basis of personality, their investigation and measurement might help to identify the particular features of vulnerability and

ANPS AND CLINICAL IMPLICATIONS

resilience in clinical patients (Davis et al., 2003; Davis & Panksepp, 2018; Montag & Panksepp, 2017; Panksepp, 2006). This could have a significant impact on clinical practice, since it might allow the enrichment of diagnostic formulation based on what emerges from the use of ANPS. For example, Clarici et al. (2015) used ANPS to assess baseline emotional functioning before and after treatment in a group of mothers with postpartum depression symptoms. This involved a treatment along with intranasal administration of oxytocin (thought to act on the basic emotional system CARE by reinforcing maternal behavior).

Because the domains of personality and psychopathology are closely related (Krueger & Tackett, 2006), the theory of AN and its operationalization by ANPS represents a fundamental *tool* for studying the emotional endophenotypes that constitute personality. The ability to identify patterns of emotional endophenotypes within the psychopathological domain (i.e., varying degrees of emotional endophenotypes shared by different psychopathological phenomena) could help us to better redefine the traditional diagnostic boundaries of heterogeneity and comorbidity.

Future directions

The use of ANPS in clinical contexts could help conceptualize psychopathological phenomena in terms of strength and weakness factors that might contribute to the development of these forms of psychopathology. Within the ANPS framework, these factors are represented by the different emotional endophenotypes. Therefore, further studies should be conducted to improve the application of the ANPS in the clinical setting.

Most of the studies discussed in this review are related to cross-sectional studies. A future area of research using ANPS in clinical contexts would require longitudinal studies that could show how the relationships between basic emotional systems evolve over time. These types of approaches could help develop a better etiological understanding in the clinical setting and observe what different factors might play a role in the development of psychopathologies or in the context of a therapeutic intervention.

ANPS AND CLINICAL IMPLICATIONS

Future lines of research are needed to further investigate and shed more light on whether ANPS can be considered an instrument that assesses emotional endophenotypes, as it presumes to do. Many such investigations are underway, and many have already been conducted (e.g., Harro 2019; Montag et al, 2016a; Plieger et al, 2014; Reuter, 2009; Sanwald et al, 2020; Savitz 2008c). The value that a tool/measure like this could have is absolutely promising for personality research as well as for psychopathological and clinical investigation.

Limitations

The review comprised some papers with incomplete psychological assessments (e.g., no use of other instruments in addition to the ANPS) and missing information (e.g., on the [sub]samples), which may affect the generalizability of the results obtained. Also, as noted by Montag et al. (2021), it would also be useful in the future to identify the gold standard among the various available versions of the ANPS to maximize the degree of consistency across studies using the ANPS.

The review paper followed PRISMA guidelines and given that authors had completed data extraction the current work is not eligible for inclusion in PROSPERO.

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ANPS AND CLINICAL IMPLICATIONS

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