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Patient personality and psychotherapist reactions in individual psychotherapy setting: a systematic review

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Abstract

Despite the importance of psychotherapists' subjective experiencse working with patients with mental issues, little is known about the relationship between therapists' emotional reactions and patients' personality problems. The present study is a systematic review of quantitative research on the association between patients' personality pathology and psychotherapists' emotional, cognitive and behavioural reactions in individual psychotherapy setting. A systematic database search (from January 1980 to August 2019) supplemented by manual searches of references and citations identified seven relevant studies. Significant and consistent relationships were found between therapist reactions and specific personality traits or disorders. In general, odd and eccentric patients tend to evoke feelings of distance and disconnection; emotionally dysregulated patients tend to evoke anxiety and incompetence, and anxious and withdrawn patients tend to evoke sympathy and concern. However, the relatively small sample of studies and methodological inconsistencies across studies limit firm conclusions and suggest the need for more systematic research. Findings from this review indicate that patients who share the same personality disorder or symptoms tend to evoke specific and similar cognitive, emotional and behavioural reactions in their therapists. This suggests that therapists overall reactions toward patients may be source of valuable diagnostic information.

KEYWORDS

 $countertransference, personality\ disorders, systematic\ review, the rapeutic\ relationship,$ $The rapist\ reactions$

1 | INTRODUCTION

1.1 | Countertransference: origins and definitional issues

The term countertransference (CT) was originally introduced by Sigmund Freud in 1909 to describe the difficulties Carl G. Jung encountered in his therapy relationship with a patient (Stefana, 2015). Specifically, Freud viewed the analyst as a blank screen onto which the patient projects his or her own internal world, and CT as an

obstacle that needed to be removed. Building on this base, early psychoanalysis simply saw CT as the analyst's unconscious and neurotic responses to the patient's transference, or rather as a barrier "induced," "aroused," "evoked" within the analyst (who was considered to be a neutral observer) by the patient (considered as the only subject). This view delineated a monopersonal outlook of the therapeutic relationship.

Starting from the late 1940s, with the original papers of Heinrich Racker and Paula Heimann (Stefana, Borensztejn, & Hinshelwood, n.d.), a gradual and widespread acceptance of CT as a tool for diagnosis and

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therapy took place, along with a more general recognition of the fact that the analyst's subjectivity and identity are inseparable from being a person with feelings and thoughts that are triggered within a bipersonal field. This view denoted a turn toward a two-person view of the therapeutic situation (Stefana, 2017), with an emphasis on paying more attention to the patient–therapist relationships.

However, despite more than a hundred years of theoretical reflections and discussion, a consensus definition of the CT construct has not yet been reached. Historically, three main conceptions of CT are identifiable as predominant among innumerable variations and transformations: the *classical*, the *totalistic*, and the *complementary* views (Epstein & Feiner, 1988). These three views form the basis of most of the existing definitions. The classical definition (e.g., Freud, 1910) posits that CT is an unconscious reaction based on the therapist's own unresolved conflicts, typically originating in child-hood and triggered by the patient's transference. These reactions can interfere with the therapist's understanding and, more generally, with psychotherapeutic process and outcome. Thus, CT is an obstacle that the therapist must avoid or overcome.

The totalistic definition (e.g., Heimann, 1950) postulates that CTs indicate all of the therapist's reactions to the patient. These reactions are normal and inevitable, and the therapist should self-investigate and use CTs to better understand both him or herself and the patient and his or her impact on other persons. Thus, the study and understanding of each CT reaction is potentially beneficial for the psychotherapeutic work. Interestingly, the totalistic position became more popular between the forties and fifties, the same decades when psychoanalytic therapists began regularly treating severely disturbed patients (borderline and psychotic: which caused strong emotional reactions in the analyst) (Gelso & Hayes, 2007; Stefana, 2017).

Finally, according to the complementary view (e.g., Levenson, 1995), CT represent the therapist's reactions that complement or counterpart to the patient's relational style. These reactions are the result of patient's manifestation of particular "pulls" on the therapist, who reacts in ways commonly expected of other people in the patient's daily life. The therapist should not act out these reactions, but ideally seeks to use them to better understand the patient's relational dynamics.

Starting from the recognition that each of these three main conceptions of CT has significant limitations but, at the same time, point to important elements of and factors related to CT, Gelso and Haves (1998. 2007) proposed an integrated definition of CT as "internal and external reactions in which unresolved conflicts of the therapist, usually but not always unconscious, are implicated" (Hayes, Gelso, Goldberg, & Kivlighan, 2018, p. 497). According to this conception, CT being useful or a hindrance to treatment depends on the degree to which therapist understands his or her CT reactions and uses them to better understand the patient. CT is an inevitable (evident in all therapists) reaction originating in the therapist's own and unresolved personal conflicts and/or unconscious vulnerabilities, and triggered by both transference and nontransference material brought in session by the patient (Hayes, Nelson, & Fauth, 2015). CT is a subset of therapist overall reactions.

Key Practitioner Message

- Patients who share the same personality features or disorders tend to evoke specific and similar cognitive, emotional and behavioural reactions in their psychotherapists
- Clusters A and B personality disorders patients evoke more troublesome emotional reactions among therapists than cluster C personality disorders patients
- Therapists' patterns of reactions toward patients with specific personality features or disorders are independent from therapist's theoretical orientation

1.2 | Empirical research on countertransference

From the early 1950s CT began to go beyond the borders of the psychoanalytic world, and the first sporadic attempts to empirically study it started (Bandura, Lipsher, & Miller, 1960; Cutler, 1958; Fiedler, 1951; Yulis & Kiesler, 1968). However, the research progressed slowly, in large part because of the fact that CT was firmly rooted in the psychoanalytic tradition, whose members mostly shared Freud's deep scepticism about the utility of empirical research; they often considered it of very little interest, if not a downright "antipsychoanalytic practice" (Ortu, 2007). Other major causes included the extreme richness and complexity of the phenomena (which inter alias encompass therapist's conscious and unconscious personality characteristics, sore aspects of his or her personal history, and emotions/thoughts/behaviours in response to the patient or to the therapeutic situation that are often difficult to tolerate and or admitsuch as those of hate or of a sexual nature), the definitional ambiguity surrounding the concept, the methodological difficulties in measuring it, and the remarkable reluctance of therapists to be under close research scrutiny (because of the shortage of time, the attribution of low scientific or clinical value to empirical research or that specific topic, or the fear of being evaluated and/or judged negatively).

However, the publication of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; APA, 1980), introducing a multiaxial system of classification that included an axis reserved for personality disorders (PDs), enhanced empirical research on CT and also motivated investigation of the possible relation between patients' PDs and clinicians' reactions or CT (Bourke & Grenyer, 2010, 2013; Brody & Farber, 1996; Eren & Şahin, 2016; Lewis & Appleby, 1988; Liebman & Burnette, 2013; McIntyre & Schwartz, 1998; Rosenkrantz & Morrison, 1992; Rossberg, Karterud, Pedersen, & Friis, 2008; Schwartz, Smith, & Chopko, 2007). Consequently, research grew from 1980 until at the turn of the new millennium there was a critical mass of empirical literature on CT suggesting its pantheoretical status, and that CT and its management were related to psychotherapy outcome. In response, CT and CT management were studied by the American

Psychological Association's Division of Psychotherapy Task Force (Division 29), whose objective was to identify empirically supported (therapy) relationships as key elements of all psychotherapy relationships. Based on the results of the review of empirical literature (Gelso & Hayes, 2001, 2002), the APA Task Force concluded that the CT management is promising and probably effective as a means of customizing therapy (Norcross, 2001, 2002).

1.3 | Psychotherapy relationship

The therapist-patient relationship, defined as "the feelings and attitudes that the counseling participants have toward one another, and the manner in which these are expressed" (Gelso & Carter, 1985), is a key aspect of the therapeutic process. Its technical (roles and methods) and relational parts are constantly and reciprocally interacting; but they are different, and the therapeutic relationship accounts for process and outcome variance in and of itself. Indeed. recent meta-analytic evidence on psychotherapy outcomes estimate that the therapeutic relationship accounts for 15% of the total variance, patient and therapist individual features account respectively for 30% and 7%, while the specific treatment method accounts for 10% (Norcross & Lambert, 2018, 2019a), Furthermore, a metaanalysis on the correlations between adult psychotherapy outcome and CT reactions (as described by the integrated definition) and their management found that CT is inversely related to outcomes, whereas the successful CT management is related to better outcomes (Hayes et al., 2018). CT is a basic part of the wider and inevitable therapist's emotional, cognitive and behavioural reaction to a patient.

1.4 | Psychotherapists' reactions and patients' personality disorders

The clinical literature is consistent in reporting that personality disordered patients evoke more troublesome and problematic emotional reactions (Bateman & Fonagy, 2006; Gabbard, 2009, 2014; Kernberg, 1975, 2004; McWilliams, 2011; Millon & Grossman, 2007a; Millon & Grossman, 2007b). These patients' recurrent interpersonal patterns (Hopwood, 2018b; Hopwood, Wright, Ansell, & Pincus, 2013; Hopwood, Zimmermann, Pincus, & Krueger, 2015) inevitably appear in the therapeutic relationship. Interestingly, the research on the emotional reactions of the therapist toward the patient started with Freud's considerations of the emotional difficulties Jung encountered in the treatment of a borderline female patient suffering from borderline PD (Hoffer, 2001).

However, there are divergent data on whether and how different PDs evoke different (either overall or CT) reactions among clinicians. This may be partially due to the fact that a number of studies have investigated the emotional reactions among different professional roles (such as psychiatrists, psychiatry residents, psychiatric nurses, social workers, art therapists, psychologists, etc.), without considering that some dimensions of patients' psychopathology may elicit

different emotional reactions among different professional roles (Black et al., 2011; Bodner et al., 2015; Bodner, Cohen-Fridel, & lancu, 2011; Eren & Şahin, 2016; Satir, Thompson-Brenner, Boisseau, & Crisafulli, 2009). This highlights the importance of differentiating clinicians in terms of the specificity of their relationship with the patients (Colson et al., 1986).

The role of subjective experiences and responses is widely considered crucial in mental health training and practice. For instance, mental professional working with challenging patients may feel a sort of rejection of their own emotional states, which in turn may have an adverse impact on therapy with a given individual as well as broader outcomes (Yakeley, Hale, Johnston, Kirtchuk, & Shoenberg, 2014). Thus, individual level factors may be important for understanding emotional, cognitive and behavioural reactions to patients with PD diagnoses. The type of psychotherapy may also influence the therapist reactions. For example, a study found that transference focused psychotherapy therapists experience more negative affect in their clinical work with patients with borderline personality disorder as compared to both dialectical behaviour therapy and psychodynamically oriented supportive psychotherapy therapists (Meehan, Levy, & Clarkin, 2012).

1.5 | Purpose of review

Given the importance of the patient–psychotherapist relationship for a successful treatment, as well as the variety of factors affecting such relationship, this review aims to provide a comprehensive evaluation on the association between patients' personality pathology and psychotherapists' emotional, cognitive and behavioural reactions in individual psychotherapy setting.

2 | METHOD

2.1 | Protocol and registration

The Cochrane Database of Systematic Reviews and the International Prospective Register of Systematic Reviews (PROSPERO) were searched to ensure no similar reviews existed. Details of the protocol for this systematic review, which followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009), may be found in PROSPERO dataset (registration number: CRD42018115199).

2.2 | Eligibility criteria

We used the following eligibility criteria: (1) published in a peerreviewed journal; (2) included samples of participants aged 18 and older (consistent with the emphasis on PDs); (3) included licensed psychotherapists (with degree in medicine or psychology); (4) investigated the psychotherapists' general (cognitive, affective or behavioural) reaction when interacting with a specific well-defined patient in an individual psychotherapy; (5) included information about the patients' specific personality trait(s) and/or disorder(s) associated with the psychotherapists' reaction; (6) formal self or observer assessments of the psychotherapist's reactions. Studies were excluded if (1) they were not quantitative designs; (2) used samples of children/adolescents; (3) used artificial stimuli (e.g., clinical vignettes or audio-recorded sessions) to elicit and then evaluate psychotherapists' reaction; (5) it was not possible to distinguish psychotherapists from the other mental health professionals (e.g., nurses, psychiatry residents); (6) involved online or telephone psychotherapy.

2.3 | Information sources

Studies were identified by searching online databases from 1980 to the present, with no language restrictions. The starting year of 1980 was selected as the publication of the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM; American Psychiatric Association, APA;, 1980). The systematic literature search was applied on August 23, 2019, to MEDLINE (24 hits) and PsycINFO (130 hits) via EBSCOhost.

2.4 | Search strategy

The following search terms were used to search for all databases:

((personality disorder) OR (personality trait) OR (personality pathology)) AND ((psychotherapist response) OR (psychotherapist reaction) OR (psychotherapist emotional response) OR (psychotherapist emotional reaction) OR (psychotherapist feeling))

- ((personality disorder) OR (personality trait) OR (personality pathology)) AND ((therapist response) OR (therapist reaction) OR (therapist emotional response) OR (therapist emotional reaction) OR (therapist feeling))
- ((personality disorder) OR (personality trait) OR (personality pathology)) AND ((clinician response) OR (clinician reaction) OR (clinician emotional response) OR (clinician emotional reaction) OR (clinician feeling))
- ((personality disorder) OR (personality trait) OR (personality pathology)) AND (countertransference OR countertransferential)

2.5 | Study selection

Study selection was performed independently by two Authors (AS and CB). Any disagreements were resolved by consensus reached through discussion. Titles and abstracts were reviewed and screened for evidence that the studies met eligibility criteria, with interrater agreement of 92%. Full-text articles were reviewed and screened to ensure consistency with the inclusion and exclusion criteria, with interrater agreement of 93%. Furthermore, the reference lists of full articles reviewed were scanned for further relevant literature (see Figure 1).

2.6 | Data collection process

A data extraction sheet was developed and pilot-tested on five randomly-selected included studies. One Author extracted the data while a second Author checked it. Disagreements were resolved by consensus. In the case of studies with unclear data, the corresponding Authors were contacted for information. The juxtaposing of both

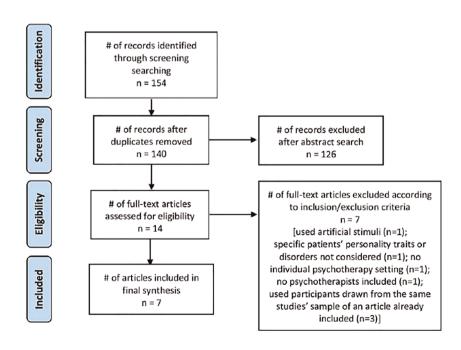


FIGURE 1 PRISMA diagram of study selection process [Colour figure can be viewed at wileyonlinelibrary.com]

Author names and sample sizes was used to discover the presence of multiple reports of the same study.

2.7 | Data extraction

The following information was extracted from each study. Study characteristics: Authors, year of publication, country; study methodology: study design, setting, data collection time points, sample size; patients' characteristics: mean age, male gender, diagnosis; therapists' characteristics: mean age, male gender, professional title, theoretical orientation; patients' personality trait/disorder: measures for the assessment; therapists' reaction: measures for the assessment; relevant findings.

2.8 | Quality assessment

All studies selected were assessed on methodological quality independently by two Authors (VB and AS) through the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (National Heart Lung, 2014). Disagreements were resolved through joint review and discussion. All studies were rated good. The results of the quality assessment are reported in Table 1, and the explanation of the calculation of the quality score for each study is available as Supporting Information (see Table S1).

2.9 | Data analysis

A narrative synthesis (Mays, Roberts, & Popay, 2001) of the included studies was performed.

3 | RESULTS

Seven primary studies were included in the review (Table 1). Three additional articles were excluded because they used participants drawn from the same studies' sample (i.e., full dataset or subsample from a larger trial) of an article already included, and did not report additional correlates.

3.1 | Study characteristics

All the included studies were published in English between 2005 and 2018. They included a large number of patients (mean = 166.14; SD = 100.20, range: 67–332) and clinicians (mean = 148.14, SD = 121.91, range: 6–322, median = 181). More than half of the included studies were conducted in Italy (57%, k = 4) (Genova & Gazzillo, 2018; Colli, Tanzilli, Dimaggio, & Lingiardi, 2014; Tanzilli, Colli, Del Corno, & Lingiardi, 2016; Tanzilli, Muzi, Ronningstam, & Lingiardi, 2017). The others were conducted in the USA (29%, k = 2)

(Betan, Heim, Zittel Conklin, & Westen, 2005; Meehan et al., 2012) and Norway (14%, k=1) (Dahl, Røssberg, Bøgwald, Gabbard, & Høglend, 2012). Five studies were cross-sectional (Betan et al., 2005; Colli et al., 2014; Genova & Gazzillo, 2018; Tanzilli et al., 2016; Tanzilli et al., 2017), and the remaining two were longitudinal (Dahl et al., 2012; Meehan et al., 2012).

The majority (57%) of the studies (Betan et al., 2005; Colli et al., 2014; Tanzilli et al., 2016; Tanzilli et al., 2017) reported a minimum length of eight sessions at the time of the therapist emotional/cognitive/behavioural assessment. One study (Genova & Gazzillo, 2018) reported at least four sessions and one further study (Meehan et al., 2012) assessed the therapist emotional/cognitive/behavioural response after four months of psychotherapy. Only one study (Dahl et al., 2012) assessed therapist emotional response after each session over the psychotherapy period starting from the first session.

3.2 | Psychotherapists characteristics

Only three studies (43%) reported the mean ages of the psychotherapists, which were 43 years (SD = 9) (Colli et al., 2014), 47 years (SD = 9.80) (Tanzilli et al., 2016), and 45.13 years (SD = 8.62) (Tanzilli et al., 2017). Six studies (86%) declared therapists gender: participants were predominantly female (52.11%, N = 542). Only two studies (29%) (Colli et al., 2014; Tanzilli et al., 2016) reported therapists' ethnicity; all the 535 therapists in these studies were white/Caucasian (100%).

With regard to psychotherapists' theoretical orientation, 543 (53%) of them were psychodynamically oriented, 347 (34%) were cognitive–behavioural oriented, 125 (12%) were eclectic, and the remaining (1%) were identified with other approaches. Regarding their clinical experience, in four studies (57%), the minimum level of experience was 3 years from psychotherapy licensure (Betan et al., 2005; Colli et al., 2014; Tanzilli et al., 2016, 2017). In one study (Meehan et al., 2012) the experience ranged from 2 to 15 years; in one further study (Genova & Gazzillo, 2018) clinicians had 10.5 (range: 1–38) years of experience; whereas in the remaining study (Dahl et al., 2012) the post-internship experience ranged from 2 to 14 years (mean = 6.5, SD = 3.28).

3.3 | Patients characteristics

In six studies (86%) (Betan et al., 2005; Colli et al., 2014; Dahl et al., 2012; Genova & Gazzillo, 2018; Tanzilli et al., 2016, 2017) patients may or not have fulfilled criteria for one or more "Axis I" (i.e., non-PD) diagnosis, while in the remaining study (Meehan et al., 2012) "Axis I" disorders were exclusion criteria. Overall, five studies used samples of patients with mixed diagnoses (71%) (Betan et al., 2005; Colli et al., 2014; Dahl et al., 2012; Genova & Gazzillo, 2018; Tanzilli et al., 2016), the remaining two studies used full samples of patients who met criteria for narcissistic PD without

					Therapist's reaction	Personality trait/disorder	Study	Quality
Study	Country	Therapists	Patients	Treatment length	measure	assessment	design	rating
Betan et al. (2005)	ASU 2	N = 181 Psy = 141; MDPsy = 40 F = 75; M = 106 Age M = NR Theoretical orientation PD = 43; CB = 37; Ec = 55 Clinical experience min 3 years	N = 181 nonpsychotic. Diagnosis: Mixed (DSM-IV) F = about one-half M = about one-half Mean age = 40.5 years	Mean		length = 19 months	Z,	DSM-IV Axis II (chart
Dahl et al. (2012)	Norway	N = 6 Psy = 1; MDPsy = 5 F = 2; M = 4 Age M = NR Theoretical orientation PD = 6 Clinical experience range 10-25 years	N = 75 nonpsychotic. Diagnosis: Mixed (DSM-III-R) F = 46; M = 29 Mean age = 37 years	Mean length = 34 sessions	FWC-58	SCID-II for DSM-III-R	_	Good
Meehan et al. (2012)	USA	N = 16 Psy = NR; MDPsy = NR F = NR; M = NR Theoretical orientation Mixed Clinical experience range 2-15 years	N = 73 nonpsychotic Diagnosis: BPD (DSM-IV) F = 67; M = 6 Mean age = 31 years	Length = 1 year	ACQ + TRQ	IPDE for DSM-IV	_	Good
Colli et al. (2014)	Italy	N = 203 Psy = 132; MDPsy = 71 F = 111; M = 92 Theoretical orientation PD = 103; CB = 100 Clinical experience mean = 10 years	N = 203 nonpsychotic Diagnosis: Mixed (DSM-IV) F = 118; M = 85 Mean age = 34 years	Mean length = about 5 months	TRQ	SWAP PD scales	S	Good
Tanzilli et al. (2016)	Italy	N = 332 Psy = 232; MDPsy = 100 F = 180; M = 152 Theoretical orientation PD = 169; CB = 163 Clinical experience mean = 10 years of psychottherapy practice	N = 332 nonpsychotic Diagnosis: Mixed (DSM-IV) F = 174; M = 158 Mean age = 40 years	Mean		length = 4-5 months	TRQ	SWAP PD scales

TABLE 1 (Continued)

Study	Country	Country Therapists	Patients	Treatment length	Therapist's reaction measure	Therapist's reaction Personality trait/disorder assessment	Study design	Quality rating
CS	Good							
Tanzilli et al. (2017)	Italy	N = 67 Psy = 41; MDPsy = 26 F = 38; M = 29 Theoretical orientation PD = 39; CB = 28 Clinical experience mean = 9.1 years of psychotherapy practice	N = 67 nonpsychotic Diagnosis: NPD without comorbid PDs (DSM-IV) F = 29; M = 38 Mean age = 37.2 years	Mean length = about 4 months	ТRQ	SWAP PD scales	S	Poog
Genova and Gazzillo (2018)	Italy	N = 232 Psy = NR; MDPsy = NR F = 154 M = 78 Theoretical orientation PD = 141; CB = 15; Ec = 70; Other = 4 Clinical experience mean = 10.5 years post-training	N = 232 Diagnosis: Mixed (PDM-2) F = 137; M = 95 Mean age = 34.8 years	Mean		length = 17.7 months	Q,	PDP-2
(PDM-2)	CS	Good						

Note: ACQ = Affective Communication Questionnaire; BPD = Borderline Personality Disorder; CB = cognitive behavioural; CS = cross-sectional; Ec = ecletic; F = female; FWC-58 = Feeling Word Checklist-58; IPDE = International Personality Disorder Examination; L = longitudinal; M = male; MDPsy = psychiatrists; NPD = Narcisistic Personality Disorder; PD = psychodynamic; PDM-2 = Psychodynamic Diagnostic Prototypes-2; Psy = psychologists; SWAP = Shedler-Westen Assessment Procedure; TRQ = Therapist Response Questionnaire.

*Twenty patients from each group had terminated the therapy at the time of data collection. comorbidity of other PDs (Tanzilli et al., 2017) and for borderline PD (Meehan et al., 2012).

3.4 | Measures used for the assessment of patients' personality pathology

Three studies used the DSM in its third (DSM-III-R; APA, 1980) (14%) (Dahl et al., 2012) or fourth edition (DSM-IV-TR; APA, 2010) (29%) (Betan et al., 2005; Meehan et al., 2012). More specifically, Dahl et al. (2012) calculated the total number of PD criteria for each patient, that is the sum of positive criteria on the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) (SCID-II; First, Spitzer, Gibbon, Williams, & Benjamin, 1994). Betan et al. (2005) asked clinicians to rate as present or absent each criterion of axis II diagnoses of the DSM-IV, and then summed the number of symptoms endorsed for each of PDs in each Cluster. Meehan et al. (2012) assessed the total DSM-IV PD Cluster symptoms through the International Personality Disorder Examination (Loranger, 1995). Further three studies (43%) (Colli et al., 2014; Tanzilli et al., 2016, 2017) assessed personality features and disorders using the Shedler-Westen Assessment Procedure-200 (SWAP-200: Shedler Westen, 2004, 2007; Westen & Shedler, 1999a, 1999b). The remaining (14%) (Genova & Gazzillo, 2018) assessed the patient's level of personality organization through the Psychodynamic Diagnostic Prototypes-2 (PDP-2; Gazzillo, Genova, & Lingiardi, 2016) based on the Psychodynamic Diagnostic Manual-2 (PDM-2) Axis P disorders (Lingiardi & McWilliams, 2017).

3.5 | Measures used for the assessment of psychotherapists' reactions

The psychotherapists' emotional, cognitive and behavioural reactions were assessed using self-rated standardized questionnaires (see Table 2). The majority of studies (86%) (Betan et al., 2005; Colli et al., 2014; Genova & Gazzillo, 2018; Meehan et al., 2012; Tanzilli et al., 2016, 2017) used the Therapist Response Questionnaire (TRQ; Zittel Conklin & Westen, 2003), one study (Meehan et al., 2012) used both the TRQ and the Affective Communication Questionnaire (ACQ; Meehan, 2004), while the remaining study (Dahl et al., 2012) used the Feeling Word Checklist-58 (FWC-58; Røssberg, Hoffart, & Friis, 2003). The FWC-58 assesses only the emotional reactions.

3.6 | The relations between patients' personality pathology and therapists' reactions

3.6.1 | Level of personality organization

Only two studies examined the psychotherapist's reactions to patients' overall level of personality organization (see Table 3). Dahl et al. (2012) found that the number of PD criteria was negatively

associated with confident and disengaged responses (i.e., more personality pathology is associated with fewer confident feelings and fewer feelings of being bored and tired with the patient). Genova and Gazzillo (2018) found that more severe patient's level of personality organization was positively associated with more a helpless and overwhelmed therapist's response and negatively associated with positive reactions.

3.6.2 | Cluster level

Three studies compared the psychotherapist's reaction in relation to personality symptoms at the cluster level (see Table 3).

Cluster A (paranoid, schizoid, and schizotypal) PDs were found to be positively associated with therapists' criticized/mistreated response, that is the feelings of being unappreciated, dismissed, or devalued by the patient (Betan et al., 2005). Likewise, in a full sample of patients who met criteria for Borderline PD, higher Cluster A symptoms were positively associated with therapists' negative affect (Meehan et al., 2012) that includes both criticized/mistreated and overwhelmed/disorganized responses.

Cluster B (antisocial, borderline, histrionic, and narcissistic) PDs found strongly associated with were to be whelmed/disorganized, helpless/inadequate, sexualized (i.e., sexual feelings toward the patient or experiences of sexual tension), and disengaged responses, while these PDs were negatively associated with positive responses (Betan et al., 2005). Similarly, in a full sample of patients with a diagnosis of narcissistic PD without comorbidity of other PDs, was found that narcissistic disordered patients with elevated levels of Cluster B personality pathology tended to evoke more negative and heterogeneous responses than narcissistic patients who did not manifest traits typical of this Cluster (Tanzilli et al., 2017). Whereas in a full sample of patients with borderline PD, Cluster B symptoms were not found to be related to any specific reaction (Meehan et al., 2012).

Cluster C (avoidant, dependent, and obsessive-compulsive) PDs were positively associated with a parental/protective response (Betan et al., 2005). However, when considering a sample of patients with borderline PD, Cluster C symptoms were negatively associated with both negative affect and an enlivened reaction (i.e., therapist's tendency to think about the patient quite a bit in between their sessions, and/or to see that patient stimulating to work with).

3.6.3 | Patients' specific personality traits or disorders and psychotherapists' reactions

Five studies investigated the role of patient's specific personality features or disorders on the psychotherapist's response (see Table 4).

Paranoid personality traits were positively associated with criticized/mistreated reaction (i.e., feelings of being criticized, mistreated or devaluated by the patient) (Colli et al., 2014; Tanzilli et al., 2016). In addition, it was positively associated with therapists'

TABLE 2 Questionnaires used for the assessment of psychotherapists' reactions.

Name	Description	Factors/Subscales
Affective Communication Questionnaire (ACQ; Meehan, 2004)	It is a 28-item self-report measure that asks therapists to rate their patients in terms of the degree to which they felt enlivened and engaged by them, the nature of the affect experienced in sessions with the patients, and the degree to which patients imbued their language with affect. Each statement is rated on a 5-point Likert scale, ranging from 1 (not true) to 5 (very true), in terms of how much the given statements characterized the therapist's work with the patient.	 (1) Disengaged factor represents therapists experiencing their patients and themselves as each feeling disengaged from the treatment; (2) full range of emotions factor represents the therapist experiencing a full range of emotion in the treatment; (3) negative affect factor represents the therapist experiencing a predominance of negative affect in the treatment; (4) enlivened factor represents therapists experiencing their patients and themselves as feeling enlivened in the treatment. Meehan et al. (2012) found the following correlations between ACQ and TRQ factors: disengaged factor correlates with disengaged (r = 0.81, p = 0.01); full range factor correlates with positive/satisfying (r = 0.44, p = 0.01); negative affect factor correlates with criticized/mistreated (r = 0.79, p = 0.01), helpless/inadequate (r = 0.67, p = 0.01), and overwhelmed/disorganized (r = 0.29, p = 0.05); and enlivened factor correlates with positive (r = 0.44, p = 0.01) and parental/protective (r = 0.36, p = 0.01) factors.
Feeling Word Checklist-58 (FWC-58; Røssberg et al., 2003)	It is a 58-item self-report measure in which therapists rate their emotional responses toward the patient on 5-point Likert scales ranging from 0 (nothing) to 4 (very much). The therapist is asked to rate to what degree they had experienced 58 feeling states.	The principal component analyses by Dahl et al. (2012) reveals four subscales: (1) confident subscale includes the following feeling states: total control, clever, overview, attentive, receptive, confident, helpful, happy, enthusiastic, calm, objective; (2) inadequate subscale includes the following feeling states: inadequate, anxious, threatened, stupid, distressed, insecure, helpless, overwhelmed, cautious, rejected, disliked, embarrassed; (3) parental subscale includes the following feeling states: motherly, affectionate, dominate, important; (4) disengaged subscale includes the following feeling states: tired of, sleepy, indifferent, aloof.
Therapist Response Questionnaire (TRQ; Zittel Conklin & Westen, 2003)	It is a 79-item self-report questionnaire designed to assess therapists' countertransference patterns in psychotherapeutic setting on a 5-point Likert scale ranging from 1 (not true) to 5 (very true). The items measure a wide range of thoughts, feelings, and behaviours experienced by therapists toward their patients.	The English version of the TRQ revealed a eight-factor structure (Batan et al., 2005): (1) overwhelmed/disorganized factor indicates a desire to avoid or flee the patient and strong negative feelings, including dread, repulsion, and resentment; (2) helpless/inadequate factor describes feelings of inadequacy, incompetence, hopelessness, and anxiety; (3) positive factor indicates the experience of a positive working alliance and close connection with the patient; (4) special/overinvolved factor describes a sense of the patient as special, relative to other patients, or describes 'soft signs' of problems in maintaining boundaries, including self-disclosure, ending sessions on time, and feeling guilty, responsible, or overly concerned about the patient; (5) sexualized factor describes sexual feelings toward the patient or experiences of sexual tension; (6) disengaged factor describes feeling distracted, withdrawn approved or borred in sessions:

withdrawn, annoyed, or bored in sessions;

TABLE 2 (Continued)

Name	Description	Factors/Subscales
Name	Description	(7) parental/protective factor describes a wish to protect and nurture the patient in a parental way, above and beyond normal positive feelings toward the patient (8) criticized/mistreated factor describes feelings of being unappreciated, dismissed, or devalued by the patient. The Italian version of the TRQ (Tanzilli et al., 2016) revealed nine dimensions which are very similar to those of the English version, with the exception of the original criticized/mistreated pattern that seems to be split into hostile/angry and criticized/devaluated factors. (1) Helpless/inadequate factor indicates feelings of inadequacy, incompetence, hopelessness, and a strong sense of inefficacy; (2) overwhelmed/disorganized factor describes an intense feeling of being overwhelmed by the patient's emotions and needs, as well as confusion, anxiety, dread or repulsion; (3) positive/satisfying factor indicates indicating an experience of close connection, trust, and collaboration with the patient resulting from a good therapeutic alliance; (4) hostile/angry factor indicates feelings of anger, hostility, and irritation toward the patient. (5) criticized/devalued factor describes a sense of being criticized, unappreciated, dismissed, or devalued by the patient; (6) parental/protective factor describes a wish to protect and nurture the patient in a parental way, above and beyond normal positive feelings toward him/her; (7) special/overinvolved factor indicates that the patient is very special, so much so that the clinician may show some difficulties in maintaining the boundaries of the therapeutic setting (e.g., more self-discloser with this patient than with other ones, or ends sessions late); (8) sexualized factor describes the presence of sexual attraction or feelings toward the patient; (9) disengaged factor describes feelings of annoyance, boredom, withdrawal, or distraction in
		sessions.

hostile/angry response and negatively associated with positive reactions (Tanzilli et al., 2016).

Schizoid personality traits were positively associated with the helpless/inadequate response (Colli et al., 2014; Tanzilli et al., 2016) and disengaged reactions (Tanzilli et al., 2016). Furthermore, schizoid personality patterns were positively associated with therapists' parental and disengaged responses (Genova & Gazzillo, 2018).

Schizotypal personality traits were positively associated with disengaged reactions (Colli et al., 2014; Tanzilli et al., 2016).

Antisocial personality traits were positively associated with therapists' criticized/mistreated/devalued (i.e., feelings of being criticized and mistreated by the patient) (Colli et al., 2014; Tanzilli et al., 2016) and hostile/angry reactions (Tanzilli et al., 2016).

Borderline personality symptoms/traits showed a positive association with the special/overinvolved reaction (i.e., a sense of the patient as special, relative to other patients, or 'soft signs' of problems in maintaining boundaries, including self-disclosure, ending sessions

18

Association between clusters of personality disorder and psychotherapists' reactions.

TABLE 3

	Betan et al., 2005	Meehan et al., 2012 ^a	Tanzilli et al., 2017 ^b	Dahl et al., 2012	Genova & Gazzillo, 201
Cluster A symptoms	Criticized/Mistreated	Negative Affect, i.e. Helpless/Inadequate Overwhelmed/Disorganized Criticized/Mistreated		Negative relationships between number of PD criteria and Confident and Disengaged reactions	helpless overwhelmed positive (in reverse)
Cluster B symptoms	Helpless/Inadequate Overwhelmed/Disorganized Positive (in reverse) Criticized/Mistreated Sexualized		Helpless/Inadequate Overwhelmed/Disorganized Positive/Satisfying		
Cluster C symptoms	Parental/Protective	Enlivened (in reverse), i.e. Positive (in reverse) Parental/Protective (in reverse) Negative affect (in reverse), i.e. criticized/mistreated (in reverse) helpless/inadequate (in reverse) overwhelmed/disorganized (in reverse)			

(SWAP-200 NPD Scale T score 60 and high-functioning scale T score 60) sample of patients had a NPD diagnosis ^aThe full sample of patients had a BPD diagnosis. ₫

without comorbidity of other PDs

on time, and feeling guilty, responsible, or overly concerned about the patient) (Betan et al., 2005; Colli et al., 2014; Tanzilli et al., 2016). Additionally, borderline personality traits were positively associated with helpless/inadequate, overwhelmed/disorganized (Colli et al., 2014; Tanzilli et al., 2016), and criticized/devalued responses (Tanzilli et al., 2016).

Histrionic personality traits were negatively associated with therapist's disengaged reaction (Colli et al., 2014), meaning that these tended to increase therapist involvement, and positively associated with sexualized reactions (Tanzilli et al., 2016). Likewise, hysterical/histrionic personality styles were positively associated with sexualized and overwhelmed/disorganized reactions (Genova & Gazzillo, 2018).

Narcissistic personality symptoms/traits showed a positive association with the disengaged reaction (i.e., to be distracted, withdrawn, annoyed, or bored in sessions) (Betan et al., 2005; Colli et al., 2014; Tanzilli et al., 2016). Furthermore, they were found positively associated with therapist's hostile/angry and criticized/devaluated reactions (Tanzilli et al., 2016). Narcissistic personality syndromes positively associated were parental/protective and criticized/mistreated responses (Genova & Gazzillo, 2018). Consistently with these results, narcissistic PD was positively associated with disengaged, hostile/angry, criticized/devaluated, and helpless/inadequate therapists' reactions, and negatively associated with the positive/satisfying response (Tanzilli et al., 2017). At the same time, narcissistic PD patients with borderline, histrionic, and antisocial personality traits elicited significantly higher helpless/inadequate and overwhelmed/disorganized reactions from clinicians than patients without these features. On the other hand, narcissistic PD patients without other Cluster В personality traits evoked significantly higher positive/satisfying responses (Tanzilli et al., 2017).

Avoidant personality traits were positively associated with a positive/satisfying, parental/protective, and special/overinvolved responses (Colli et al., 2014; Tanzilli et al., 2016). Similarly, anxious personality patterns were positively associated with parental and disengaged reactions (Genova & Gazzillo, 2018).

Dependent personality traits were positively related to therapists' parental/protective helpless/inadequate, and special/over-involved reactions (Colli et al., 2014; Tanzilli et al., 2016), and negatively associated with therapist's disengaged reaction (Colli et al., 2014), meaning that these personality traits tended to increase therapist involvement. A further study that evaluated dependent personality styles found that they were positively associated with parental/protective and disengaged responses (Genova & Gazzillo, 2018).

Obsessive-compulsive personality traits were negatively associated with the therapist's special/overinvolved response (Colli et al., 2014), and positively associated with disengaged reactions (Tanzilli et al., 2016). These latter reactions were found to be associated also to obsessive-compulsive personality styles (Genova & Gazzillo, 2018).

TABLE 4

	DSM-IV-TR SWAP-200 PD Scales	PDM-2 PDs	Betan et al., 2005	Colli et al., 2014	Tanzilli et al., 2016	Tanzilli et al., 2017 ^a	Genova & Gazzillo, 2018
Cluster A	Paranoid	Paranoid		Criticized/Mistreated	Positive/Satisfying (in reverse) Hostile/Angry Criticized/Devalued		
	Schizoid	Schizoid		Helpless/Inadequate	Helpless/Inadequate Disengaged		Parental/protective Disengaged
	Schizotypal			Disengaged	Disengaged		
Cluster	Antisocial	Psychopathic		Criticized/Mistreated	Hostile/Angry Criticized/Devalued		
	Borderline	Borderline	Special/Overinvolved	Helpless/Inadequate Overwhelmed/Disorganized Special/Overinvolved	Helpless/Inadequate Overwhelmed/Disorganized Criticized/Devalued Special/Overinvolved		
	Histrionic	Hysteric- Histrionic		Disengaged (in reverse)	Sexualized		Overwhelmed/Disorganized Sexualized
	Narcissistic	Narcissistic	Disengaged	Disengaged	Hostile/Angry Criticized/Devalued Disengaged	Helpless/Inadequate Positive/Satisfying (in reverse) Hostile/Angry Criticized/Devalued Disengaged	Criticized/Mistreated Parental/Protective
Cluster	Avoidant	Anxious		Positive Special/Overinvolved Parental/Protective	Positive/Satisfying Special/Overinvolved Parental/Protective		Parental/Protective Disengaged
	Dependent	Dependent		Helpless/Inadequate Special/Overinvolved Parental/Protective Disengaged (in reverse)	Helpless/Inadequate Special/Overinvolved* Parental/Protective		Parental/Protective Disengaged
	Obsessive- Compulsive	Obsessive- Compulsive		Special/Overinvolved (in reverse)	Disengaged		Disengaged

^aThe full sample of patients had a primary NPD diagnosis without comorbidity of other personality disorders. In their article, Tanzilli and colleagues reported also the bivariate correlations between TRQ factors and SWAP-200 each PD scale.

3.6.4 | Patients' psychological functioning and symptoms severity

The studies investigating the relationship between the psychotherapist's pattern of responses, the patients' psychological functioning, and their severity of symptoms showed inconclusive results. In particular, two studies (Dahl et al., 2012; Tanzilli et al., 2017) found no significant correlations between the therapist's response factors and either psychological functioning or symptom severity, while two other studies (Colli et al., 2014; Tanzilli et al., 2016; but see also Lingiardi, Tanzilli, & Colli, 2015) found a positive correlation or a partial mediation effect.

3.6.5 | Psychotherapist's theoretical orientation

All the studies (Betan et al., 2005; Colli et al., 2014; Tanzilli et al., 2016, 2017) that verified whether therapists' patterns of reactions toward patients with specific personality features or disorders were influenced by therapist's theoretical orientation showed that the results were independent from clinicians' theoretical beliefs.

4 | DISCUSSION

To our knowledge, this is the first systematic review of the empirical literature reporting on the association between the psychotherapists' emotional, cognitive and behavioural reactions and the patients' personality features or disorders. The main finding is that the included studies are consistent in showing that different personality patterns elicited different but quite consistent reactions across the psychotherapists.

At a the cluster level (see Table 3), positive partial correlations were found between Cluster A (the 'odd, eccentric' cluster) PDs and psychotherapists' feelings of being unappreciated, dismissed, or devalued by the patient (Betan et al., 2005; Meehan et al., 2012), whereas Cluster B (the 'dramatic, emotional, erratic' cluster) PDs were mainly associated with therapists' feelings of inadequacy, incompetence, hopelessness and anxiety, and their desire to avoid or flee the patient and strong negative feelings (including dread, repulsion and resentment) (Betan et al., 2005; Tanzilli et al., 2017). Interestingly, Meehan et al. (2012) found no relationship between Cluster B symptoms and therapists' reactions, but it should be noted that all patients in that study met criteria for BPD, so ceiling effects could have obscured such relationships. Finally, Cluster C (the 'anxious, fearful' cluster) PDs were associated with therapists' wish to nurture and protect their patient in a parental way in one study (Betan et al., 2005), and with therapists' low negative affect and their characterizing the treatment as less enlivened in another study (Meehan et al., 2012). These results are in accordance with the clinical literature suggesting that clusters A and B PDs patients evoke more troublesome emotional reactions among therapists than cluster C PDs patients (Gabbard, 2014; McWilliams, 2011). Furthermore, empirical studies excluded from this review and involving group therapists (Rossberg et al., 2008), psychiatrists (Pallagrosi, Fonzi, Picardi, & Biondi, 2016) and various mental health workers (Eren & Şahin, 2016; Thylstrup & Hesse, 2008) confirmed these results in relation to the clinicians' patterns of reactions to Cluster B patients, but show contradictory results about the clinicians' reaction toward Cluster A and Cluster C patients. Our findings align with a review of empirical studies focused on clinician reactions to patients with eating disorders (Thompson-Brenner, Satir, Franko, & Herzog, 2012), suggesting that clinicians' negative reactions toward patients with eating disorders usually reflected frustration, hopelessness, lack of competence, and worry. However, experienced psychotherapists reported lower levels of negative feelings than inexperienced therapists or trainees. Moreover, clinicians' negative emotional reactions in regard to patients with eating disorders appear to vary according to the patient's personality pathology.

With regard to the relationship between therapist overall reaction and patient personality pathology, each study included in this review found significant and consistent relationships between therapists' responses and specific personality traits or disorders (see Table 4). However, despite significant overlapping associations, there are some differences among the findings from these studies. Notably, future research may shed more light on these issues by isolating the specific patient features that evoke therapist reactions, particularly if it uses evidence-based dimensional models of personality disorder that distinguish severity from style and that organize stylistic features around individual differences in personality (Hopwood, 2018a; Hopwood et al., 2018). The studies included in this review that used the SWAP-200 as a measurement tool provide an instructive example. Here it is interesting to report that a recent study that investigated the relationship between therapists' reactions and patients' personality pathology using three different dimensional models of personality at the same time (all empirically derived from the SWAP-200: two relying on distinct versions of the five factor model, and another based on a multifaceted model of personality syndromes), found that therapists' reactions are coherently and systematically associated with patients' personality features (Tanzilli, Lingiardi, & Hilsenroth, 2018).

Regarding the associations between therapist's pattern of responses, patients' psychological functioning, and their severity of symptoms showed, it seems to us that since the signs were not flipped in the null studies than the results could be framed as evidence suggesting small to moderate associations.

Overall, our results suggested that patients who share the same personality features or disorders (and thus share similar ways of feeling, thinking, and behaving) tend to evoke specific and similar cognitive, emotional and behavioural reactions in their psychotherapists. These associations seems to be independent from both patients' non-diagnostic characteristics and psychotherapists' approaches and methods or years of professional experience. This allows to hypothesize the existence of 'objective' reactions, which we can define as the therapist's response for the patient based on the real and specific types of personality disturbance of the patient. Our hypothesis is consistent with some psychoanalytic theorizations, such as the one proposed by Winnicott, 1949), who, based on his clinical experience with

borderline and psychotic patients, posited a type of CT that is authentically objective in direct response to the patient's objective personality and behaviour. Additionally, Winnicott identified a type of CT influenced by the analyst's personal characteristics (thought to be rooted in his/her own particular developmental experiences) that make his/her being with that specific patient qualitatively different than that of any other analyst. The existence of slight differences in the reactions to patients with similar personality profiles founded in this review, leads us to hypothesize, in line with Winnicott, the existence also of 'subjective' reactions, which are what we call CT (see the Introduction section). These subjective reactions could in fact rely on the individual therapist's life history and, at least partially, on the quality of the psychotherapy training received (i.e., personal psychotherapy and clinical supervision experiences). These subjective reactions are a between-therapist variable. And since the CT is specific to each therapist, it is unexplained variance that will not be observable in the effect sizes reviewed here. With regard to the objective reactions, they can be useful for understanding patient's personality features and his or her impact on others, whereas the successful management of the subjective reactions (which can happen only if the therapist is able enough to recognize and tolerate his or her emotional conflicts and vulnerabilities) is related to better psychotherapy outcomes (Hayes et al., 2018). The combination and interaction of the objective and subjective elements result in the overall reaction detected in the studies reviewed. Furthermore, it seems that when working with patients with personality features or disorders, the objective component generally has a greater proportional impact on the therapist's overall reaction than the subjective one. However, it should be mentioned that that also might be an artefact of objective factors being easier to measure in traditional research designs.

In addition, this helps explain why therapists' patterns of reactions toward patients with specific personality features or disorders were independent from therapist's theoretical orientation (Betan et al., 2005; Colli et al., 2014; Tanzilli et al., 2016, 2017). Curiously, despite empirical data indicating that mental health workers (including psychotherapists) who had had a personal psychotherapy experience report lower levels of difficulty while working with PD patients than colleagues who did not have had a psychotherapy experience (Eren & Şahin, 2016), none of the reviewed studies explored the role of therapist's personal psychotherapy experience.

There are a number of caveats to the present review, mainly due to the limitations of the included studies. An important limitation of the studies included is the dearth of data on the broader spectrum of variables pertaining to the therapist and their possible mediating/moderating role. The variables most commonly examined are age, gender, theoretical orientation, and clinical experience level, much more than other personal characteristics and/or interpersonal functioning and skills – such as, for example, humility, flexibility, empathic ability, emotional awareness, quality of personal life, etc. – which represent the most common sources of an important part of the emotional reactions (Hayes et al., 1998) and which show direct effects on treatment outcomes (Heinonen & Nissen-Lie, 2019; Lingiardi, Muzi, Tanzilli, & Carone, 2018). Another limitation is that the

data sets were often not ideal to study therapists' reactions, as they usually only include one or very few patients per therapist, thus not allowing statistical modelling of the possible therapist effect (Castonguay & Hill, 2017) on outcome. A further main limitation is the cross-sectional design of the studies, which does not allow evaluating if and how the therapist's reactions change during the psychotherapeutic journey. For example, it is plausible that the objective reaction will undergo changes only to the extent that the patient's personality has changed, while the subjective reaction will be more linked to the therapist's inner and outer experiences. In the absence of longitudinal data, we are not able to determine whether and how the therapist's emotional reaction is an acute emotional response originated by patient's characteristics, or a chronic emotional response caused by the therapist's unresolved issues/characterological difficulties, an emotionally bad day, or both. Another limitation is that all studies reviewed used self-report measures that may have important limits related to insight and objectivity. Finally, it should be noted that patient diagnoses were based on different diagnostic tools.

Two further limitations of the current review should be acknowledged. The search terms used might not have identified all studies. Furthermore, due to the few number of studies included and their heterogeneity of methods and outcome measures, it was not possible to perform a quantitative meta-analysis.

A pivotal future direction in this research will be to explore more fully the relationship between therapist's reactions patterns and other components of the therapeutic relationship, such as therapeutic alliance and real relationship (see Norcross & Lambert, 2019b), as well as to explore if and how this variable influences psychotherapy process and outcome. Furthermore, it would be valuable to triangulate on both therapists' reactions and patients' personality pathology by using multi-informant (e.g., measures rated by both the therapist and an independent observer or supervisor) and multi-method (e.g., measures rated by the therapist/observer/supervisor and detected with neuroscientific techniques) approaches. Because therapist reactions are partially unconscious phenomenon, at least for part of the diagnostic/therapeutic journey, and it would be difficult for the therapist him/herself to grasp and measure solely via self-report. Finally, future studies should investigate longitudinally the specific weight of the interlocking elements (i.e., the subjective and the objective) of the therapist's reaction considering the professional, personal and interpersonal characteristics of both therapists and patients in order to have a better and deep understanding of what is inside the therapist's overall reaction, and of its diagnostic and/or therapeutic usefulness.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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