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Review of Psychodynamic Psychotherapy Neuroimaging Studies

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Key Words

Neural correlates · Brain imaging · Functional magnetic resonance imaging · Single-photon emission computed tomography · Positron emission tomography · Psychodynamic psychotherapy · Depression · Anxiety

Abstract

The clinical efficacy of psychodynamic psychotherapy (PDT) has undergone extensive study and review. Recently, researchers have studied the effects of this treatment on brain metabolic or synaptic activity, but the collective findings have never been reviewed. The objective of this review was to describe the findings of all neuroimaging studies of any form of PDT treatment. An extensive literature search through databases along with surveying of research groups were undertaken to acquire all available published studies. Eleven series were included in the final sample, consisting of 2 randomized controlled trials, 5 controlled trials and 4 case series, altogether involving 210 people: 94 healthy controls and 116 people with mood disorders, panic disorder, somatoform disorders and borderline personality disorder. A variety of neuroimaging techniques were used to examine regional metabolic activity and synaptic neurotransmission before and after treatment. The common finding was normalization of synaptic or metabolic activity in limbic, midbrain and prefrontal regions, occurring in association with improved clinical outcomes. PDT has demonstrable effects on brain function in diverse clinical populations as evidenced by a modest group of mixed neuroimaging studies.

Introduction

Psychodynamic psychotherapy (PDT) has recently undergone extensive study, meta-analysis and review [1]. The clinical benefits of this therapeutic approach are now supported by meta-analyses of randomized controlled trials across mood [1], somatoform [2], personality [3] and mixed disorders [4]. The outcome literature, therefore, demonstrates an empirical foundation for the clinical efficacy of PDT. However, neuroimaging exploration of the brain substrates of these effects has only recently begun.

Reviews of the neuroimaging markers of effects of psychotherapeutic modalities, including cognitive behavioral therapy (CBT) and interpersonal therapy, have recently been published. In general, such reviews have documented normalization of baseline abnormalities, defined as no significant differences compared with expected norms or with nonpsychiatric comparison subjects on the relevant measure, after successful psychotherapy. Further, neuroimaging changes were associated with symptom reduction [5–9]. These studies have implicated spe-

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cific brain regions involving affect-regulatory systems (amygdala, insula, orbital prefrontal cortex and subgenual cingulate cortex), memory (hippocampus) and procedural memory systems (basal ganglia), as well as attentional and conscious self-reflective systems (dorsal prefrontal regions) [10].

A systematic review of neuroimaging studies of anxiety and depressive disorders compared the changes in cerebral metabolic activity after successful treatments with selective serotonin reuptake inhibitors (33 studies) or with CBT (30 studies) [5]. Both treatment approaches normalized metabolic activity in brain regions typically implicated in these disorders. However, pharmacological treatments mainly tended to reduce baseline overactivity in ventral prefrontal and limbic structures, while CBT mainly tended to increase baseline hypoactivity in dorsal prefrontal regions.

Another comprehensive review focused on the neurobiological effects of different psychotherapy approaches with major depressive disorder [6]. After successful CBT (7 studies), interpersonal therapy (3 studies) and PDT (1 study), normalization of metabolic activity was detected in several brain regions including the amygdala as well as prefrontal and cingulate cortices.

In this study, we reviewed neuroimaging studies involving PDT. This psychotherapy focuses on identifying and addressing unconscious feelings, impulses and conflicts that result in a broad range of symptoms and personality problems. By recognizing these processes and working through the emotions, patients can theoretically be freed from the effects of the past, become able to form healthy relationships, and experience a marked reduction in symptoms [1]. We hypothesized that PDT would have brain effects that parallel clinical improvement.

Methods

Methods and results are reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement [11].

Selection (Inclusion Criteria)

We compiled all available neuroimaging studies reporting on baseline and posttreatment measures after PDT treatment in non-brain-damaged adults and published in English or with English abstracts until August 2013.

Search Procedures

An electronic search was performed using PubMed Medline, PsycINFO and Web of Science databases with the following key words: 'psychodynamic', 'psychoanalytic', 'psychotherapy', 'treatment', 'therapy', 'neuroimaging', 'PET', 'SPECT', 'SPET', 'fMRI', 'functional neuroimaging' and 'brain imaging'. A request was also sent to a membership-based forum of psychotherapy researchers for articles on this topic including in-press articles. Reference lists of articles were explored for further relevant articles.

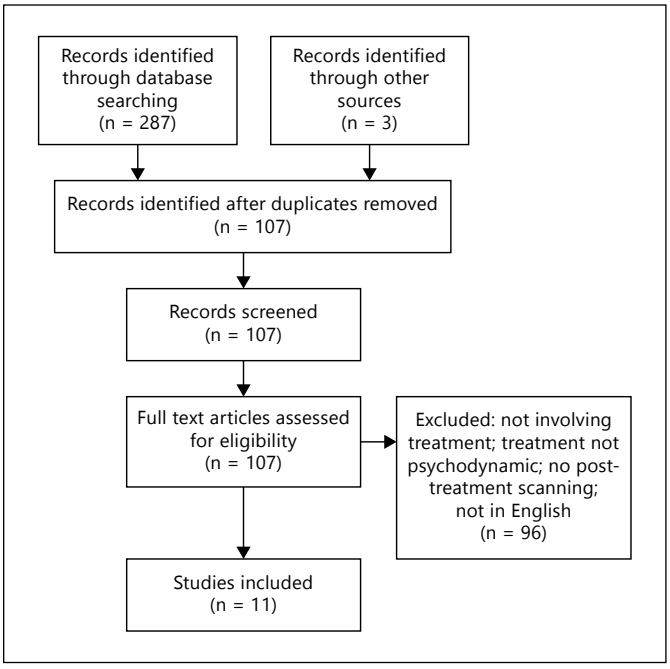

Fig. 1. Summary of report selection.

Data Collection and Assessment of Methodological Quality

Consensus agreement that a paper met the inclusion criteria was required between two authors in order to finally include it in this review. Data were extracted and interpreted by two authors, and all authors reviewed the articles as a crosscheck on accuracy of interpretation of the data.

Results

Description of Studies

The search identified 107 articles in total, after removing duplications and articles of the same series. Of these, 96 series were excluded because they involved no treatment, or the treatment was not psychodynamic, or the language was different from English. Eleven series were included in the final selection, involving a total of 210 people (116 with mental illness and 94 healthy controls) and a range of psychiatric illnesses including depression (atypical and typical), mixed depression, borderline personality disorder, panic disorder and somatoform disorder. The series consisted of 2 randomized controlled trials [12, 13], 5 controlled trials [14, 15] and 4 case series [16–

Table 1. Direction of differences in synaptic neurotransmission after Psychodynamic Psychotherapy

	Clinical condition		Baseline[1]	Ref. No.		After treatment[1]	Ref. No.
Midbrain	Depression	↓	SERT (9)	[20–22]	↑	SERT (16)	[13, 20–22]
	Hypomania	↑	SERT (1)	[21]	↓	SERT (1)	[21]
Thalamus	Depression	↓	SERT (1)	[22]	↑	SERT (1)	[22]
	Depression				=	$D_2/_3$ binding (8)	[12]
	Depression				↓	$D_2/_3$ binding (14; after fluoxetine)	[12]
Medial prefrontal	Depression	↓	SERT (2)	[22]	↑	SERT (2)	[22]
Subgenual/subcallosal prefrontal	Depression				↑	5-HT_{1A} (8)	[17]
Midtemporal	Depression				↑	5-HT_{1A} (8)	[17]
Striatum	Depression	=	DAT (8)	[21, 22]	=	DAT (21)	[13, 22]
	Depression				=	$D_2/_3$ binding (8)	[12]
	Hypomania	↑	DAT (1)	[21]	↓	DAT (1)	[21]

DAT = Dopamine transporter binding; SERT = serotonin transporter binding; 5-HT_{1A} = serotonin receptor binding; $D_2/_3$ = dopamine D_2/D_3 receptor.

[1] Values in parentheses denote numbers across studies.

19]. The search is illustrated in figure 1 (see online suppl. tables 1, 2; for all online suppl. materials, www.karger.com/doi/10.1159/000358841).

Treatment interventions were classified as PDT when defined by a manualized treatment protocol with established efficacy or by clear criteria outlined in the methodology, involving interventions focusing on unconscious conflicts as they emerge in the therapeutic or transference relationship. The number of psychotherapists providing treatment interventions varied from 1 to 16 for series conducted in outpatient settings, and was unspecified in the 2 series conducted in inpatient settings. Five series described the formal training and experience of the therapists [12–14, 17, 18].

Treatment settings included outpatient clinics for 8 series, with individual psychotherapy sessions occurring either once a week [12, 13, 16, 19, 20] or multiple times per week [14, 17, 18]. These treatments involved from 16 to 120 h of PDT treatment spread over 4–16 months. The other 3 series were conducted in inpatient settings [15, 21, 22] where mixed interventions along with individual PDT were employed over a period of 35–80 days.

The neuroimaging methods used in these series included single-photon emission computed tomography, positron emission tomography and functional magnetic resonance imaging [23]. After treatment, all included series reported group improvement from baseline clinical symptoms. Normalization of baseline scores was achieved in 8 series [12, 13, 15, 16, 18, 20–22]. In 1 series [17], some features of borderline personality disorder remained after treatment, but the participants no longer met diagnostic criteria. In another series [14], group baseline scores significantly improved with treatment, but 5 of 16 participants still fulfilled diagnostic criteria for major depressive disorder at the treatment endpoint.

Posttreatment Neuroimaging Changes Relative to Baseline

The 5 functional neuroimaging series reported improvement in regional brain activation levels in response to emotionally or motivationally significant stimuli after PDT (table 1; online suppl. tables 1, 2). In 1 series [15], posttreatment patients with panic disorder responding to emotionally valenced words showed no difference compared with controls: increased metabolic activity was observed in the ventral and orbital prefrontal regions, along with decreased activity in temporal regions. In a second series [14], posttreatment patients with depression had metabolic activity similar to controls in regions of the amygdala, hippocampus and dorsal prefrontal cortex in response to attachment-related stimuli: treated cases had less activation than controls in the subgenual cingulate cortex. In a third and fourth series [21, 22], patients with somatoform disorders showed significant enhancement toward normalization and relative to controls in differential blood flow between anticipation of reward versus an-

ticipation of no reward in regions of the postcentral gyrus, dorsal anterior cingulate, occipital cortex and ventroposterior thalamus. When presented with empathy paradigms versus control paradigms, patients showed significant enhancement toward normalization of brain activity with the emotion of anger in regions of the parahippocampal gyrus, amygdala, superior temporal gyrus, posterior insula and postcentral gyrus. Finally, 2 patients with borderline personality disorder responded to a psychological stress condition at the posttreatment time point with levels of regional metabolic activity in frontal and limbic areas similar to the pretreatment quiet condition, indicating lower levels of perceived stress; moreover, increased perfusion in frontal areas in response to stress following treatment was associated with improved impulse control [16].

Synaptic Neurotransmitter Studies

The 6 series of synaptic neurotransmission reported improvements toward normalization in neuroimaging measures after PDT (table 1; online suppl. table 2). Increased midbrain serotonin transporter binding (SERT) toward normalization or control values was observed in an aggregate total of 16 patients with either atypical depression [13], severe-to-moderate depression [17, 18] or borderline personality disorder with mild depression [19]. Increased SERT was also found in the medial prefrontal cortex of 1 patient with depression, and in the medial prefrontal cortex and thalamus of 1 patient with borderline personality disorder with mild depression [19]. On the other hand, a single case of dysthymia and hypomania [18] showed a decrease (normalization) in midbrain SERT after treatment. With regard to dopamine transporter binding densities, normal baseline and posttreatment levels were found in the striatum of patients with atypical or typical depression [13] and in the limbic structures of patients with depression [13, 19]. However, striatal dopamine transporter binding densities decreased toward normalization for the case with depression and hypomania [18]. In 1 positron emission tomography series, dopamine D_2/D_3 receptor binding assessed in patients with depression remained stable in the thalamus and striatum after PDT treatment, while it increased with antidepressant medication (fluoxetine) in the lateral thalamus [12]. In a separate series of the same sample, the 5-HT_{1A} receptor binding potential increased significantly in a depression group after treatment with PDT, with an effect size of 0.85 across brain regions; the brain regions involved the dorsal, subgenual and subcallosal anterior cingulate gyrus and midtemporal region [20]. This increase in 5-HT_{1A} receptor binding was not seen in patients treated with fluoxetine, despite similar clinical improvement in both clinical groups. In patients who had reached remission (HAM-D score ≤7) after PDT (n = 4), posttreatment increase in 5-HT_{1A} receptor binding strongly correlated with improvement in HAM-D depression ratings. Treatment with fluoxetine brought no significant changes in 5-HT_{1A} receptor binding in this group, and no more changes than observed in controls [20]. In a later analysis, Karlsson et al. [24] found that this increase in 5-HT_{1A} receptor binding correlated with improvement in social adjustment in the PDT group, but not in the fluoxetine group.

Discussion

This review compiled findings from a series of diverse neuroimaging series showing brain functional and neurochemical changes in response to PDT. In the four disorders studied, patterns of neural activity or neurophysiological infrastructure in regions of the dorsolateral prefrontal cortex, orbital frontal cortex, anterior cingulate cortex (ACC) and amygdala differed between clinical cases and healthy controls prior to treatment, while after treatment, the patterns seen in patients resembled those of the controls. As the posttreatment changes in baseline measures of brain function correlated with improvement in clinical presentation, these neurobiological changes appear indicative of improvement on a biological level [12–19, 21, 22]. Such improvements in neuroimaging measures might reflect neural correlates of the changes effected by PDT and expressed clinically as symptom reduction [1–4].

It is notable that activity levels in brain circuits that appear to be involved in processes of interest to psychodynamic theory appear aberrant in pathological states and show improvement after a course of PDT. While much remains to be understood about what these patterns of activity revealed by neuroimaging means on a functional level [25], it is possible to speculate about some of the findings summarized in this review. For example, baseline overactivity in regions associated with emotion may relate to activated but unprocessed emotions that are brought to consciousness during PDT [14, 15, 21, 22]. In depression, posttreatment reduction in regional activity in the subgenual ACC – an area associated with guilt [26], self-defeat [27] and repression of emotions [28] – may reflect overcoming of repression of emotions and reduction in unconscious guilt, thus resulting in a better relationship with oneself and antidepressant effects [14]. In

borderline personality disorder cases, improvement in dorsolateral prefrontal cortical function may reflect a transition to more mature defenses with PDT [16]. Such findings warrant replication and a priori hypothesis testing to examine the neuroimaging changes observed when specific PDT processes take place.

With the advent of neuroimaging studies of different psychotherapy models such as PDT and CBT, researchers may generate testable hypotheses about which baseline neuroimaging markers relate to treatment response when these different models are used [29]. For example, the finding by Buchheim et al. [14] that PDT was effective in depression cases with subgenual ACC overactivity, where others have found that CBT [30] and CT [31] do not appear to be effective in such cases, is of interest and may warrant formal study. Such efforts to use imaging data to predict treatment outcomes is in its early stages and requires standardization of methodologies before robust baseline treatment predictors can be identified [29].

In the same vein, one can now use neuroimaging to study the effects of treatment ingredients common to different therapy models, such as levels of adherence, therapeutic alliance or emotion activation [32, 33]. Combined, such neuroimaging research may help clarify the relationships of treatment variables to both short- and long-term outcomes toward elucidating what works for whom.

This review has a number of limitations rendering its findings preliminary. First, the numbers of series and included patients were small. Second, not all series included healthy subjects to control for effects of time and repeated testing. Third, there was variation in imaging methodologies between series. Fourth, the reviewed sample included diverse populations and diagnostic categories. Fifth, a mix of psychodynamic therapeutic models may have been used in these series, and the frequency of sessions and duration of treatment were variable across series. Finally, although most PDT treatments were the sole treatment provided in an outpatient setting, other series were part of integrated treatment efforts in inpatient settings; hence, other factors may have accounted for the observed changes. Therefore, the findings of these studies are currently insufficient to build any models of consistent changes in brain structure and function associated with psychodynamic treatment; nevertheless, the summary of these findings provided above may serve as a foundation for further exploration.

In conclusion, there are preliminary data showing that PDT correlates with specific neurobiological changes in diverse populations. Further research is indicated to study brain changes both within PDT [31] and between psychotherapy models in order to help identify specific therapeutic ingredients operating within specific populations.

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Disclosure Statement

The authors use psychodynamically oriented psychotherapy with a variety of clinical populations.

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