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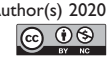

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# Future Applications of Real-World Neuroimaging to Clinical Psychology

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**Abstract**

Clinical neuroimaging has largely been limited to examining the neurophysiological outcomes of treatments for psychiatric conditions rather than the neurocognitive mechanisms by which these outcomes are brought about as a function of clinical strategies, and the cognitive neuroscientific research aiming to investigate these mechanisms in nonclinical and clinical populations has been ecologically challenged by the extent to which tasks represent and generalize to intervention strategies. However, recent technological and methodological advancements to neuroimaging techniques such as functional near-infrared spectroscopy and functional near-infrared spectroscopy-based hyperscanning provide novel opportunities to investigate the mechanisms of change in more naturalistic and interactive settings, representing a unique prospect for improving our understanding of the intra- and interbrain systems supporting the recogitation of dysfunctional cognitive operations.

**Keywords**

Psychotherapy, ecological validity, neuroimaging, clinical psychology, functional near-infrared spectroscopy, executive function, mental disorders

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## Introduction

The marked expansion of neuroimaging research and instrumentation over the past 30 years has been remarkable, and exceedingly so when considering the body of neuroscientific knowledge that has amassed from it. As Poldrack et al. (2012) noted in the case of functional magnetic resonance imaging (fMRI), it was possible in the mid-1990s to read all the literature on fMRI in a week; today, it is impossible to do this with the number of papers published last week alone. What is more is that this rapid development in neuroimaging shows little sign of decelerating. In recent years, there have been steady advances to techniques such as functional near-infrared spectroscopy (fNIRS) that potentially offer unique contributions to the cognitive neuroscientific enterprise of mapping information-processing models of the mind onto the structural and functional properties of the brain. Specifically, the real-world applications of fNIRS overcome limitations common to other neuroimaging techniques, enabling researchers to traverse novel frontiers in experimental design and brain science (see Pinti et al., 2018a, 2018b, for reviews). And perhaps the greatest utility of using neuroimaging methods in naturalistic situations will be an enhanced ecological sensitivity to clinically relevant phenomena. A common framework of techniques used in the study of neurological and psychopathological disorders has been to collect brain data periodically in laboratory settings throughout the course of treatment rather than continuously in clinically representative ones. This design is strong in its ability to assess the effects of a given intervention overtime, but it leaves an explanatory gap between treatment and outcome: Implementations of the neurocognitive mechanisms by which these effects are brought about are not measured. So, the corollary of having little ecological validity in clinical neuroimaging paradigms is a loss in the ability to capture the larger picture—as it were—of component processes involved not only in engendering these observed, neurophysiological changes but also in facilitating healthier, more adaptive thinking, feeling, and behaving. Newer neuroimaging techniques such as fNIRS are now being used in the same ways as other methods to investigate, for example, etiopathogenic mechanisms and cortical dysregulation, and the effects and efficacy of psychopharmacological treatments (see Ehlis et al., 2018, 2014; Irani et al., 2007, for reviews); however, to make the leap toward better understanding the nature and treatment of the pathogenesis of psychopathological symptoms at the level of the brain, real-world neuroimaging techniques ought to be integrated into multimodal experimental designs developed specifically for the ecological investigation of the clinical neuroscientific questions of interest. Therefore, the present article describes the concept of ecological validity, fNIRS as an emerging neuroimaging method, current challenges in clinical psychology and cognitive neuroscience to studying mechanisms of change, and future applications of real-world designs and methods that can address these issues in theory and practice.

## Onto the world

Do recent cognitive neuroscientific advancements to the understanding of human brain (dys)function from laboratory research map onto the brain as it is found and operates in the nature? The extent to which experimental designs, tasks, and methods represent observable functions at the level of the person and generalize in their predictability of responding in everyday-life situations is the degree to which they are valid, *ecologically* (Burgess et al., 2006). Traditional experimental psychology has long been criticized for using paradigms that fail to reflect the natural, everyday-life situations upon in which the forms of cognition such as memory and attention are called (e.g., Neisser, 1976). Cognitive neuropsychology has largely addressed these criticisms (Shallice, 1988), with a multitude of neuropsychological tests for assessing acquired and developmental deficits having been developed as formalized versions of real-world activities (e.g., Burgess et al., 1998). Interestingly, tasks which have taken a more ecological approach in their development are equally psychometrically sound and more predictive of the ways in which people (un)successfully interact with their environments to attain goals (see Burgess et al., 2006, for review). However, human neuroimaging has largely been lacking in this respect for a number of reasons (see Shamay-Tsoory & Mendelsohn, 2019, for review). One is that neuroimaging is the newest methodology in the arsenal of the cognitive neuroscientist and, consequently, the majority of studies have elected preexisting tasks from traditional experimental psychology to validate brain–behavior relations with these techniques. Another is that the testing environments of neuroimaging laboratories are inherently foreign and unnaturally restrictive to participants, highlighting a rudimentary limitation in the ability to even contrive of tasks which better represent real-world thinking, feeling, and behaving. That neuroimaging tasks are not highly ecological does not suggest that they all ought to be: Some tasks developed to investigate, for example, low-level (i.e., automatic) processes need not to be so markedly redeveloped as to better recruit the base-region localizations of the subsystems of interest; that is, flashing checkerboard and finger-tapping designs are sufficient stimuli to elicit basic sensory and motor systems in the occipital and parietal lobes, respectively. But many important neuroscientific questions postulate information processing systems which are highly complex and dynamic, such as those functioning to help people appropriately adapt to novel situations and act in interpersonal ones, and are not so straightforwardly captured by computer-mediated stimulus designs. Without further advancements in experimental design and methods toward a more ecological cognitive neuroscience, researchers risk limiting the component processes they are able to investigate of a given functional architecture. For example, to what extent can the uniquely human subsystems enabling spatial navigation be understood in so far as neuroimaging research is unable to elicit the situations in which the brain fully integrates the multifaceted information

concomitant to navigation such as idiothetic information? See Park et al., 2018, for a review of differential findings in this domain between laboratory and real-world testing. Critically, some cognitive neuroscientific theories are scientifically unfalsifiable in so far as experimental designs do not allow for the real-world stimuli that are integral to them; so, a theory about the unique neural bases of human-to-human interaction (e.g., Di Paolo & De Jaegher, 2012) is best tested using an experimental design capable of including additional conspecifics. However, ecological experimental designs and tasks cannot properly test predictions if researchers are unable to make multimodal observations in the real-world situations they represent. Therefore, the option to select a valid and reliable neuroimaging technique that can meet the demands of a given paradigm will be crucial to a more ecological cognitive neuroscience.

One promising method is fNIRS. There are a number of fNIRS reviews on its inception (e.g., Ferrari & Quaresima, 2012), basic principles (e.g., Gervain, 2015; Lloyd-Fox et al., 2010), statistical analysis (Tak & Ye, 2014), and quality control (e.g., Orihuela-Espina et al., 2010), as well as on current devices (Pinti et al., 2018b), research in cognitive neuroscience (e.g., Cutini et al., 2012; Masataka et al., 2015), and future directions (Pinti et al., 2018a; Quaresima & Ferrari, 2019).As with other neuroimaging techniques such as fMRI, fNIRS is predicated on the principle of neurovascular coupling, which refers to the relationship between neuronal firing mechanisms and metabolic mechanisms such as cerebral blood flow; so, observed changes in hemodynamics are used to indirectly index changes in brain activation (Villringer & Dirangl, 1995). fNIRS does this safely and noninvasively through the optical imaging technique of using near-infrared light to observe task-related changes in hemodynamics. More specifically, biological tissue is rendered transparent to near-infrared light in the spectral window of 650 to 1000 nm (Villringer & Dirangl, 1997), and when this light is emitted from sources of an fNIRS device into the cerebral cortex (3–3.5 cm), some is absorbed, some is scattered, and some returns to the detectors.Pairs of sources and detectors form channels, and most fNIRS systems are now multichannel (Bakker et al., 2012). The modified Lambert–Beer law (see Delpy et al., 1988; Kocsis et al., 2006) accounts for light absorption and scattering in biological tissue: $A = \mathrm{Log}(I_o/I) = \varepsilon_\lambda \cdot c \cdot d \cdot B + G$, where A is light attenuation, $I_o$ is the incident light intensity, I is the detected light intensity, $\varepsilon$ is the absorption coefficient of the chromophore, c is the concentration of the chromophore, d is the distance between the points where light enters and leaves the tissue (cm), B is the differential pathlength factor for the effect of scattering on pathlength, and G is the attenuation factor for tissue heterogeneity—a factor which is typically assumed *a priori* in continuous-wave fNIRS (Chiarelli et al., 2019). fNIRS systems can employ a range of different techniques of illumination (Gervain, 2015), but continuous wave is the most frequently adopted approach in cognitive neuroscience, whereby near-infrared light is constantly emitted at two or three different wavelengths (e.g., 780 nm, 805 nm, and 830 nm) into the scalp. In

short, the principles of light attenuation enable researchers to accurately convert spectroscopic measurements of optical density to task-related changes in hemodynamics (i.e., $\Delta A = \Delta\, c \cdot \varepsilon \cdot d \cdot B$), specifically to concentrations of oxygenated hemoglobin ($HbO_2$), deoxygenated hemoglobin (HbR), and total hemoglobin ($Hbt = HbO_2 + HbR$). Finally, once these data are collected in a given experiment, the signals from each channel are processed in ways similar to other neuroimaging techniques: The signals are corrected for motion artifacts, denoised of physiological, systemic influences, and built into a general-linear model for statistical inference; however, it is worth noting that there are many finer aspects and, indeed, challenges to fNIRS signal processing that differ considerably from other neuroimaging methods (see Tak & Ye, 2014, for review).

A number of studies over the last three decades have cross-validated fNIRS with other methods including positron emission tomography (e.g., Hoshi et al., 1994; Villringer, Minoshima, et al., 1997), electroencephalography (EEG; see Chiarelli et al., 2017, for review), magnetoencephalography ( e.g., Huppert et al., 2017), and fMRI (e.g., Cui et al., 2011; Heinzel et al., 2013; Noah et al., 2015; Okamoto et al., 2004; Sato et al., 2013). For example, Noah et al. (2015) developed a protocol for conducting multimodal experiments with fNIRS and fMRI to ensure signal comparability, and tested it using a complex, yet naturalistic motor task; particular software and hardware modifications were also discussed. Importantly, the temporal and spatial resolutions of fNIRS represent an adequate compromise between that of fMRI and EEG, respectively: That is, it has greater temporal resolution than fMRI, but not EEG, and greater spatial resolution than EEG, but not fMRI (Pinti et al., 2018b). It is worth noting that because neuroimaging methods differ in important ways relative to each other, the appropriateness of a technique for a given study depends on the scientific question in hand and, ideally, the optimal approach is probably a multimodal one that can capture the most advantageous aspects of several neuroimaging methods, including additional physiological measures such as eye gaze, heart rate, breathing rate, and so forth (e.g., Noah et al., 2020; see Chiarelli et al., 2017, for review). The particular questions for which fNIRS is well-suited are neuroscientific predictions of the specialization of function of subregions in the outer cortex whose task-related elicitation requires on the part of participants either unrestricted movements or human-to-human interaction. For example, fNIRS systems have seen a considerable and rapid rise in technological advancement in recent years, such as to the development of wearable, portable systems (see Pinti et al., 2018a, for an exhaustive review of studies using this class of device). These systems enable participants to freely perform tasks without the constraints common to other neuroimaging methods and researchers to investigate situations that are difficult to contrive in laboratory settings, providing an unprecedented opportunity to study complex cognition more naturalistically (e.g., Pinti et al., 2015; Stuart et al., 2019; but see Vitorio et al., 2017). Another recent advancement is fNIRS-based hyperscanning, a technique by

which fNIRS measures hemodynamic changes and interpersonal brain synchronization between two or more individuals while engaging in tasks in naturalistic or laboratory settings (see Crivelli & Balconi, 2017; Redcay & Schilbach, 2019; Scholkmann et al., 2013, for reviews). Recent research has showed that fNIRS-based hyperscanning is able to robustly assess everyday interpersonal interactions between people in ecologically valid environments (Cui et al., 2012; Dommer et al., 2012; Duan et al., 2013; Funane et al., 2011; Hirsch et al., 2018; Holper et al., 2012; Jiang et al., 2012; N. Liu et al., 2016; Y. Liu et al., 2017; Noah et al., 2020; Nozawa et al., 2016; Piva et al., 2017; Tang et al., 2015). So, researchers are now taking advantage of the relatively new neuroimaging technique of fNIRS to actively exploring novel ways in which to study domains such as social neuroscience, neurological disorders, neurorehabilitation, brain–computer interfaces, cognitive development, exercise science, and more (see Cutini et al., 2012; Herold et al., 2018; Naseer & Hong, 2015; Pinti et al., 2018a; Soltanlou et al., 2018; Strait & Scheutz, 2014; Yeung & Chan, 2020). In sum, it seems the calls for greater ecological validity in research are starting to be answered (Burgess et al., 2006; Neisser, 1976).

## The ecological problem of clinical neuroscience

However, there are some research domains that have yet to benefit from recent advancements in cognitive neuroscience. One area of particular importance is the study of psychiatric treatment—and not of the resultant efficacy or effectiveness of particular treatment modalities, but rather of the mechanisms by which healthier thinking, feeling, and behaving are brought about (i.e., mechanisms of change). While research on the etiopathogenesis of psychopathological symptoms typically involves investigating complex interactions between various classes of vulnerabilities, or diatheses, such as genetic, neurodevelopment, and cognitive factors, and stressful environmental and social factors, as well as assessing similarities within a particular class of psychopathology and differences between nonclinical populations, current clinical science frameworks investigating the treatment of such symptoms generally begins with the selection of one or more different methods to quantify cognitive, emotional, behavioral, and neurophysiological outcomes of specific forms of treatment such as pharmacological and psychotherapy (e.g., cognitive-behavioral therapy (CBT)-based forms of psychotherapy) interventions, including combined treatments, to investigate changes in these measures over time (Barlow et al., 2018). The broad experimental design of collecting these data at different points in time such as before and after treatment is powerful, in that it allows for the inference that differences in posttreatment measures are attributable to or a function of the intervention of interest, and using a multitude of methods to collect these measures creates a more complete account of the effects of a given intervention on individuals at different levels of scientific explanation, but this approach of

taking *periodic* measures and relying on traditional psychometric and neuroimaging methods seriously limits the ability of researchers to investigate the mechanisms of change.

More specifically, psychometric and behavioral measures, as well as other assessments on the part of clinician, provide useful information and can be administered quickly, but these methods are inherently challenged in their scientific explanatory power. Theoretical progress is always at stake in so far as only these techniques are used to develop and test clinical models of change, in that these classes of data cannot be used to infer the psychological mechanisms of clinical change, since there are no *psychological* mechanisms—only neural ones; thinking, feeling, and behaving are enacted nowhere else than in the human brain. Therefore, neuroscientific principles are requisite for theoretical constraint in understanding the changes facilitated in clinical settings (Tryon, 2014) and, consequently, models developed from these measures are ultimately unfalsifiable (see Popper,1956/2002). So, this means that neuroscientific methods are crucial to mapping information processing models of change onto the functions and structures of the brain. And, indeed, there are a number of research domains entirely dedicated to studying different aspects of psychopathology that adopt neuroimaging methods, such as those investigating links between genetics and structural abnormalities, atypical brain development, dysfunctional cortical regulation and connectivity, diagnostics and outcome prediction, and so forth. However, studies in clinical cognitive neuroscience on the treatment of psychiatric conditions link changes in regional metabolic activity and synaptic neurotransmission with the cognitive and emotive outcome measures that indicate decreases in dysfunctional thought operations and emotional reactivity and increases in protective factors and regulatory strategies, which is important to better understand the ways in which these changes in the brain relate to improved well-being, but the functional architectures engendering these changes throughout the course of treatment remain unclear. For example, psychotherapy for depression facilitates—among other subregions—increased activity in left rostral anterior cingulate cortex compared to before treatment (e.g., Sankar et al., 2018), suggesting that this subregion might have underwent adaptive changes that play a role in the task of downregulating negative emotion, but what isolable subsystems in the brain—that were presumably engaged during treatment, and elicited on the part of the clinician—engendering these functional changes? The limitation, here, in experimental design: Such neuroimaging studies are able only to observe outcomes of interventions rather than the operations facilitating them. So, research investigating these effects is necessarily carried out independently of clinical setting. If clients are participating in a study in which they need their brains periodically scanned (e.g., before and after treatment), they typically attend appointments to neuroimaging laboratories. This is in large part due to the practical challenges inherent to investigating brain activity in clinical settings, which has really not been a viable option in the last three

decades, and it is unclear how it would be a reliable approach if it was. Therefore, this paradigm of testing psychopathological populations on emotion regulation strategies to investigate brain regions that are hyperactive or hypoactive, or weak in functional connectivity with other regions (see Hariri, 2015), and examining the ways in which these trends change as a function of time (i.e., treatment), is unable to logically infer from these observed changes the networks supporting them during treatment.

Because neuroimaging is not conducted while clients engage in psychotherapy-based treatments, cognitive neuroscientists interested in studying mechanisms of change have instead largely focused on one of the most important factors of psychotherapy: emotion regulation (Gross, 2014a). The idea has been to develop experimental tasks that require clinical and nonclinical populations to engage in various regulation strategies to downregulate and upregulate negative and positive emotions, with some of these strategies being postulated as being the closest to those used in clinical settings and, therefore, most appropriate to studying dysregulation, namely, cognitive reappraisal. Reappraisal involves attributing a new meaning—that is, a new appraisal or affective valuation—to a goal-incongruent situation (Gross, 2014b), and a number of fMRI studies have investigated the neural correlates of the cognitive change that reappraisal purportedly brings about (Braunstein et al., 2017; Buhle et al., 2014; Messina et al., 2015; Ochsner & Gross, 2005, 2008; Ochsner et al., 2012). Such neuroimaging research that has investigated cognitive change from a general framework of human functioning and from the context of emotion dysregulation has found that reappraisal relates negatively with psychopathological symptoms and is an adaptive strategy for attenuating them (see Johnstone & Walter, 2014; Ochsner & Gross, 2014, for reviews). Although reappraisal paradigms have used tasks appropriately designed to elicit the downregulation of negative emotion, they poorly reflect the clinical strategies by which the reappraisal of goal-incongruent events is encouraged and inculcated in practice; they do not represent the means by which dysfunctional appraisal and schema processes (Lazarus, 2001; Scherer et al., 2010) are modified and, in consequence, contribute little to a cognitive neuroscientific understanding of the mechanisms driving the process of change during treatment. More specifically, the operational definition of reappraisal has varied across neuroimaging studies, with some paradigms using reappraisal as a reinterpretation tactic; whereas others have used it as a distancing tactic: Reappraisal as conceptualized as reinterpretation involves imagining negative stimuli in a neutral or positive light, finding the silver lining, as it were, and distancing as reappraisal requires participants to adopt the perspective of a detached observer. These different tactics are apt to differ in their cognitive resource demands of the subsystems that support them, which would be evidenced by variation of activity across brain regions, and, indeed, this has been found in some cases (see Ochsner et al., 2012). This is informative and not necessarily an issue in so far as the aim is not

to quantify the change mechanisms of some of the most effective treatments for psychopathology such as CBT-based forms psychotherapy. The domain of reappraisal research fails to capture the fact that the process of cognitive change is necessarily linguistically mediated in clinical practice and, crucially, the dialectical nature of verbal intervention: the *disputation process* (e.g., Beal et al., 1996; Beck, 1976; Ellis, 1962, 1994; David et al., 2010). Requiring participants to view stimuli of creepy spiders, crying strangers, and burning buildings in a more positive light to assess, for example, the modulatory role of prefrontal subregions in downregulating limbic reactivity is a markedly different thing than having them actively identify and dispute their irrational beliefs about personally relevant, goal-incongruent events, and to form more semantically adaptive propositional attitudes about them. In sum, the limitations of current experimental designs and tasks in clinical cognitive neuroscience suggest a general problem of ecological validity, hindering an improved understanding of the neural correlates of the restructuring of dysfunctional cognitive operations.

## A way forward

It is the principles of cognitive restructuring with which cognitive neuroscience ought to confer itself if neuroimaging research on cognitive change is to be representative of and generalize to the information processing systems engaged during treatment in clinical populations, and which ultimately explain observed changes in outcome measures. A potentially useful subject with which to begin addressing this issue of ecological validity is the process of change as it is understood across the theory and practice of psychotherapies in clinical psychology. From this outset, the first issue is that there are hundreds of different types of psychotherapies that vary widely across a number of factors; so, cognitive change means something different to different schools of thought. Perhaps, the only thing they all have in common is the normative element of aiming to cultivate some form of change that improves well-being in the everyday lives of clients. For example, CBT has long been a highly efficacious treatment for virtually all psychiatric conditions, but there is discordance within CBT-based theories on what cognitive processes are most proximal or distal to psychological dysfunction or are most deleterious or prophylactic to one's constitution, and what are considered the proper objects of change (e.g., dysfunctional cognitive processes) or the techniques employed to achieve it (see Austad, 2008).

However, these different viewpoints are not necessarily incommensurable; rather, they might generally describe the same phenomena, and perhaps the most insightful account will eventually come from a field that represents a confluence of the different levels of scientific explanation: cognitive neuroscience. Moreover, they are nonetheless unified on a number of important, rudimentary principles. First, CBT-based forms of psychotherapy generally share the major aim of deconstructing dysfunctional cognitions and cultivating functional ones

to treat psychopathology (Hofmann, 2014). That is, they share the common psychotherapeutic framework of cognitive restructuring (see Clark, 2014, for review), and this framework primarily depends on therapist-led efforts to strengthen cognitive change strategies that target the dysfunctional cognitions engendering emotional distress and maladaptive behavior (Clen et al., 2014). Second, CBT-based psychotherapies hold the presupposition on which this restructuring framework is based, namely, that dysfunctional cognitive processes are corrigible, or cognitively penetrable (Bermúdez, 2005; David et al., 2010). A third major principle on which all forms of CBT are predicated is cognitive mediation. This is the now ubiquitously accepted idea that the mind (i.e., information processing) mediates the relationship between stimulus and response (Ashcraft & Radvansky, 2010; Kandel et al., 2013; Ward, 2015). Perhaps, the earliest example of a psychological model propounding the idea of cognitive mediation is Woodworth's (1918) stimulus-organism-response model. Today, the most influential cognitive mediation model in psychotherapy is Ellis' (1962, 1994) activating event-belief-consequence model, which propounds that dysfunctional cognitions mediate the relationship between goal-incongruent events and distressing emotional, behavioral, and physiological responses; however, the idea itself can be traced as far back as Epictetus. So, the diathesis-stress models of psychopathology posited in CBT-based theories are cognitive-vulnerability models (Barlow et al., 2018). Thus, the principles of cognitive restructuring, penetrability, and mediation help to form a broad theoretical account of cognitive change that can explain its outcome corollaries: Clinicians identify in clients the dysfunctional appraisals and schema underlying emotional distress and maladaptive behavior and work to so dialectically challenge these processes as to cultivate rational thinking habits that encourage the expression of healthy negative emotions and help prevent client's from obstructing their future goals.

So, at the level of information processing, this likely involves manipulating semantic representations of dysfunctional cognitions in more posterior regions of the cortex rather than simply downregulating subcortical ones. In fact, the principles of appraisal theory—on which much emotion regulation research is predicted—suggest that a great deal of cognitive change in clinical settings is *offline*, in that goal-incongruent stimuli are not actively occurring in the environment, and the aim is to employ reappraisal as disputation to affective valuations about antecedent "activating events" rather than to downregulate the affective responses to active stimuli (i.e., online regulation). This means that reappraisal via the disputation of thought processes probably places greater and qualitatively different cognitive resource demands on brain regions associated with the semantic network. Interestingly, the role of such regions have previously been underappreciated in emotion regulation research (Messina et al., 2016), with recent meta-analytic research having demonstrated an important role of parietal and temporal subregions that are recruited by existing

reappraisal tasks (Messina et al., 2015). This also means that reappraisal tasks in cognitive neuroscience are using stimuli that do not represent personally relevant, activating events, and it is unclear how cognitive neuroscientists could contrive of a stimulus design that would; however, it is common practice for clinicians to identify and facilitate reappraisal of such situations. Interestingly, these are the individuals who are adept at carrying out reappraisal as disputation—not the clients. The clients require much psychoeducation to learn to cultivate this skill and independently use it in their everyday lives (Crum, 2019), but the clinicians are already regularly and expertly engaged in this cognitive task; so, these are the brains that a more ecological approach to investigating clinical change should not neglect. But what would such an approach look like?

Investigation of the information processing dynamics governing the relationship between treatment and outcome measures, such as those supporting the restructuring of dysfunctional cognitive processes, would be premature and rather impractical in so far as its approach attempts to bring neuroimaging methods into clinical settings. Instead, the nature of clinical settings and, importantly, the interpersonal interactions within them ought to be better represented at the level of experimental design and task development in clinical cognitive neuroscience. Then, research could work to fractionate the subsystems supporting the *task* of clinicians' brains to engender functional changes in that of clients. Thus, a multiperson neuroscience approach is requisite (see Redcay & Schilbach, 2019). And, as discussed above, since this task and the broader interpersonal interaction poorly reflects reappraisal as it is currently operationalized in cognitive neuroscience, such an investigation needs at least some theoretical progress to precede it toward developing a basic model of the critical construct (s) of verbal intervention in psychotherapy. For example, these interventions are necessarily linguistically mediated; so, speech production and comprehension form a large part of this interpersonal discourse. Moreover, this discourse is dialectical or normative in nature on the part of the clinician, in that sometimes the aim is to challenge the epistemological veracity of clients' beliefs against the principles of logic, empiricism, and pragmatism. The semantic network has above been postulated as important to this task, but what of the subsystems modulating these semantic representations? What executive functions in the prefrontal cortex (PFC) are recruited for it, and how should the task of these functions be generally conceptualized? One possibility is that the specific subtask of "reappraisal as disputation" within the interpersonal discourse is an ill-structured, verbally mediated reasoning problem for the PFC (Shallice & Cipolotti, 2018) and for which novel hypotheses need to be generated and tested (Shallice & Cooper, 2011) about the erroneous nature of clients' propositional attitudes (Bermúdez, 2005). If this is the case, then neuroscientific predictions of the spatial localizations of the various subtasks involved in verbal interventions can be put forward for a prospective study investigating them; for

instance, one might expect the particular involvement of rostral PFC (Brodmann's area 10; Burgess, Dumontheil et al., 2007; Burgess, Gilbert et al., 2007) right inferior frontal gyrus (pars orbitalis; Brodmann's area 47; Goel et al., 2009, 2007). So, experimental designs would need to be developed specifically for the type of treatment of interest and its subtasks would need to be structured to reflect the various stages of interaction typically occurring between clinicians and clients. This would markedly improve the ecological validity of a line of research interested in investigating mechanisms of change in clinical treatments and, more specifically, in linking these mechanisms at the neurobiological level of scientific explanation with that of cognitive theorizing. Many of the advantages of electing to use more ecological designs have recently been discussed at length by Shamay-Tsoory and Mendelsohn (2019). One possibility is to begin with fractionating interventions into agent-specific epochs of speaking, listening, and "thinking": Namely, an epoch for periods during which a client utters dysfunctional appraisals about goal-incongruent events, one for the clinician who is listening to this at the same time, one for the period during which the clinician is not listening, but thinking of what it is about these propositions that render them irrational, one for the vocalization of the clinician's reasoning, and one for period during which the client listens to this disputation. A blocked or mixed design could straightforwardly account for these epochs in a seminaturalistic clinical setting. But what are the appropriate methods and procedures for carrying out an experimental design tailored to capture clinically relevant phenomena?

Of the thousands of neuroimaging studies that have adopted methods such as fNIRS, the number of papers using this technique to study neuropsychiatric illness and clinical treatment represent less than 1%; however, there has recently been a noticeable upsurge in these areas of research, as evidenced in the two reviews on this subject (Ehlis et al., 2014; Irani et al., 2007). Irani et al. reviewed fNIRS studies on neurological diseases and psychiatric conditions, with Ehlis et al. (2014) focusing more on the latter. The clinical conditions in these reviews included traumatic brain injuries, epilepsy, neurodegenerative disorders, Parkinson's disease, attention-deficit/hyperactivity disorder, autism spectrum disorders, schizophrenia, mood disorders, anxiety disorders, personality disorders, eating disorders, and substance dependencies. The more recent review explicated a number of clinical research areas to which fNIRS is presently being applied, namely, to the description of cortical alterations in psychiatric syndromes (i.e., hypoactivity, hyperactivity, functional connectivity, etc.), the assessment of life-time brain function development, the evaluation of therapeutic effects and efficacy, the imaging genetics of psychiatric symptoms, and the development of improved diagnostics and outcome predictions. In other words, the present state of fNIRS regarding its applicability to clinical psychology is not markedly different from the ways in which other neuroimaging methods are being used in these research domains. However, with respect to the domain of

evaluating the effects and efficacy of clinical treatments for psychopathological symptoms, the fNIRS research has leaned mostly on studies of pharmacological interventions, with a few other studies involving treatments using repetitive transcranial magnetic stimulation (e.g., Dresler et al., 2009), eye-movement desensitization and reprocessing (Ohtani et al., 2009), and animal-assisted therapy (Aoki et al., 2012). However, no fNIRS studies to date have been conducted to investigate mechanisms of change in psychotherapy and, therefore, an important possibility for the future application of neuroimaging to clinical psychology is to employ this technique that is particularly well-suited for use in more naturalistic testing environments.

Wireless, wearable fNIRS devices, in particular, might be used in naturalistic settings that capture the essence of these clinical situations. Such a paradigm is able to overcome the ecological limitations of other neuroimaging methods such as fMRI by allowing participants to sit and speak normally as agents, unconstrained and undistracted by a loud, foreign machine. Other techniques and physiological measures such as EEG and heart and breathing rate, respectively, can also be integrated to improve the temporal resolution and signal-to-noise ratio. And, critically, because investigating only the brains which are the object of cognitive change will not render a full picture—as it were—of the underling mechanisms of change, the hyperscanning method can meet the need for a multiperson neuroscience approach to properly study the directional, interpersonal information processing dynamics between individuals. A number of fNIRS-based hyperscanning studies have recently explored within-brain functional changes and cross-brain synchronization during verbal communication in naturalistic settings (e.g., Hirsch, et al., 2018; Jiang et al., 2012; N. Liu et al., 2016; Y. Liu et al., 2017; Nozawa et al., 2016), revealing a multitude of brain regions involved in natural dialog and which are uniquely dedicated to interpersonal interaction. This area of research might be particularly useful in adapting these hyperscanning approaches to investigate interpersonal discourse of a more dialectical nature. And similar designs can be tuned further to quantify the precise neurocognitive mechanisms supporting different facets of the process of cognitive change. At a commonsense level of psychological explanation, this means examining the neural correlates of when individuals are gaining insight into the mediating role of their dysfunctional cognitions between goal-incongruent events and emotional distress, when they engage in the challenging of these cognitions against rational criteria, and when they reject the propositions subsequently discerned as irrational, as well as during the updating of the association of a goal-relevant situations with newly adopted, adaptive valuations. Importantly, researchers aiming to develop designs that do not depend on computer mediation and are more naturalistic in eliciting meaningful interpersonal interactions might adopt brain-first statistical approaches to recovering the stimulus design from the data (see Pinti et al., 2017); rather than inserting an *a priori* stimulus design into a complex ecological situation, this approach

recovers the onsets and durations of functional events from the real-world *a posteriori*.

Understanding the neural correlates of this recogitation of thought is important not only to cognitive theorizing in clinical cognitive neuroscience but also to the implications they might have within treatment. For example, because one of the core tenants of CBT-based forms of psychotherapy is to so educate clients to become adept at identifying and disputing their dysfunctional thoughts as to be able to independently do so long after the conclusion of treatment (e.g., David et al., 2010), it is possible that the trends in activation in clinicians brains during this task would not markedly differ from those in posttreatment clients on verbal intervention tasks—should they be developed. Another implication is the potential interaction between the systems driving verbal interventions and factors which have long been known to have a critical role in explaining outcome measures such as the therapeutic relationship (see Freeman, 2014, for review). Interestingly, one study to date has explored this using fNIRS *in situ*, namely, Y. Zhang et al., (2018) recently used the hyperscanning method to investigate interpersonal brain synchronization associated with the therapeutic alliance, finding that cross-brain coherence was strongest in the right temporoparietal junction (TPJ). This is in line with meta-analytical, fMRI findings that the TPJ is involved in semantic network changes during reappraisal (Messina et al., 2015). Unfortunately, this study did not use a specific treatment or clinicians of a particular form of psychotherapy, or a clinical population, and the testing sessions were not fractionated into clear subtasks and the analysis methods precluded scientific inferences relating to directional synchronization. However, this is nonetheless a promising direction for future research; more refined paradigms could address these issues and help to further close the theory-practice gap (Dobson & Beshai, 2013). Moreover, exploring the influence of the therapeutic alliance, or bond, on treatment strategies and outcome measures with neuroimaging techniques stands to be complimentary to other recent findings of physiological synchronization of heart rate and breathing rate between clinicians and clients (Tschacher & Meier, 2019; see also Palumbo et al., 2017). Another possibility is use wavelet coherence analysis (X. Zhang et al., 2020) as an index of the degree to which practitioners are effectively engaged with clients. In addition, interesting differences between experienced and less experienced clinicians can be explored (see Leff et al., 2007, in the case of surgeons). Such an enterprise could refine treatment protocols, guide clinical training, and enhance outcome predictions. Researchers interested in investigating mechanisms of cognitive change in real-time, but for practical reasons do not have access to hyperscanning, have the option of using the relatively new innovation of computer-based therapy. A number of reviews and meta-analyses have assessed the efficacy of internet-based CBT (iCBT), suggesting its effective for reducing mild-to-moderate psychopathological symptoms (Andersson & Cuijpers, 2009; Andrews et al., 2018; Cuijpers et al., 2009; Ebert et al., 2015;

Heber et al., 2017; Richards & Richardson, 2012; Richards et al., 2018; Williams et al., 2013). Although the researcher loses the multiperson neuroscience framework with investigating the neural underpinnings of these treatments, the potential application of real-world neuroimaging, here, would be to have a somewhat more controlled, laboratory-based setting in which to investigate particular features of iCBT-based interventions; for example, observing changes in PFC hypoactivity relative to controls during interventions designed to target depressive symptoms (see Joormann & Siemer, 2014). This is by no means an exhaustive list of the ways in which real-world neuroimaging might be applied to clinical psychology, but rather is an outline of some potential research paths toward better investigating neurocognitive mechanisms of change.

## Conclusions

In sum, there seem to be a number of challenges with which clinical cognitive neuroscientific research is faced in studying the mechanisms mediating the relationship between treatments and outcomes. The major limitations are in experimental design and ecological validity. Collecting data periodically such as before and after a given treatment is useful in examining its effects on outcome measures, but preludes inference from observed changes between these periods to the mechanisms driving change within them and, moreover, the paradigms in which neuroimaging data are collected poorly represent the clinical environments in which these changes are brought about and use tasks that fail to reflect treatment strategies for restructuring dysfunctional appraisal operations. The above task analysis of these clinical strategies suggests that tasks ought to be developed which place less emphasis on the online downregulation of affective responding and more on the semantic richness of epistemologically challenging maladaptive conceptual valuations. Addressing these issues requires experimental designs that can contrive ecologically valid situations and methods capable of continuously collecting data from the interpersonal interactions within them. fNIRS is well-suited for capturing complex cognitive processes in the real world and, therefore, is an appropriate apparatus by which to address these theoretical and practical issues. Future studies employing fNIRS in more clinically representative settings and with structured substasks of the components of a given intervention stand to potentially contribute unique insights into the governing dynamics of social and cognitive systems involved in change, especially those electing to use the hyperscanning technique. This is because the tasks of clinicians' brains are as important to understand as that of clients, including potential interactions between brains, and will likely be key to a more comprehensive account of the nature of the subsystems engendering change. A multimodal approach to fNIRS-based hyperscanning involving integrated EEG and other physiological measures will further compliment such an account. These are promising directions toward which clinical cognitive neuroscience might work to not

only improve mental health and the efficiency of clinicians but also our understanding of how people get and *stay* better. It can be expected that novel, real-world neuroimaging applications will emerge in concordance with future advances in ecological experimental design, task development, and data analysis.

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