A permutation test to probe the statistical significance of sudden gain frequency: An application
to patterns of change in cognitive and interpersonal therapy for depression

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Abstract

Objectives: Sudden gains were first identified in cognitive therapy (CT) for depression to characterize large and stable improvements. They have subsequently been studied in at least 50 studies across a range of disorders and treatments. There is evidence that sudden gains are reliably associated with positive treatment outcomes. Nonetheless, simulations have suggested that sudden gains may occur spuriously. We propose the use of a permutation test to yield a p -value to ascertain whether sudden gains occur above and beyond the level that can be expected by chance in a given sample.

Methods: We reanalyzed the study by Lemmens et al. (2016) to explore the utility of a permutation test for the occurrence and effects of sudden gains. We permuted session-by-session depression scores within each session before identifying sudden gains to explore the effects of the number of identified sudden gains. We also permuted sudden gains status. For both analyses we resampled 10,000 random datasets.

Results: In the permuted samples, the mean number of identified sudden gains was 29.43, replicating prior work that suggests caution about the occurrence of sudden gains. However, this rate was lower than the number of gains ($n = 52$) occurring in the original data ($p < 0.001$). The association between sudden gains and outcomes was also above and beyond chance level ($p < 0.001$).

Discussion: These data suggest that sudden gains occur above and beyond chance level. We provide code for these analyses and updated the suddengains R package to facilitate replications and further method development.

Keywords: Depression, mechanisms, psychotherapy, sudden gains, idiographic change patterns

Public Health Significance Statements: Sudden gains in cognitive and interpersonal therapy for depression can occur by chance. Their frequency in this study appears to be above and beyond chance level and they were associated with better outcomes. This suggests that sudden gains represent a clinically meaningful change process for a substantial subgroup of participants. When studying sudden gains, the use of a within-session permutation test to probe statistical significance may be appropriate.

A permutation test to detect the clinical and statistical significance of sudden gains: An application to cognitive and interpersonal therapy for depression

It is widely appreciated that whereas the efficacy of psychotherapy is well-established, the mechanisms that account for this efficacy are not well-understood (Kazdin, 2007; Lemmens, Müller, Arntz, & Huibers, 2016; Lorenzo-Luaces, German, & DeRubeis, 2015). One way of uncovering mechanisms of change is by focusing on patterns of change in therapy that may be discontinuous, for example depression spikes or sudden gains (Hayes, Laurenceau, Feldman, Strauss, & Cardaciotto, 2007; Keller, Feeny, & Zoellner, 2014; Tang & DeRubeis, 1999). Tang and DeRubeis (1999) coined the term “sudden gains” to characterize a pattern of change in cognitive therapy (CT) for depression that was absolute in magnitude, large relative to the severity of preceding symptoms, and stable (i.e., an average higher pattern succeeded by stably lower scores). In their study, patients who experienced a sudden gain experienced superior outcomes at the end of treatment, on average, relative to patients who did not experience a sudden gain. When followed over time, these patients had lower rates of relapse than patients who did not experience sudden gains. Moreover, using observer ratings of taped session content, Tang and DeRubeis found that patients experienced more cognitive changes in sessions preceding sudden gains than in a control session. Taken together, these data suggest that sudden gains have prognostic significance and may also help in uncovering mechanisms of change in therapy.

Since their initial proposal to account for change in CT for depression, sudden gains have been widely studied in other disorders and treatments settings, so much so that there are meta-analytic reviews focused on sudden gains. In the latest review of 50 studies ($n = 6355$), patients who experienced sudden gains had better outcomes, on average, than those that did not (Shalom

& Aderka, 2020). Some studies have reported that theory-specific mechanisms of change precede sudden gains, including hope in CT for chronic depression (Abel, Hayes, Henley, & Kuyken, 2016), agreement to behavioral change in behavioral activation (Andrusyna, 2007), and interpretations in supportive-expressive therapy (SET; Andrusyna, Luborsky, Pham, & Tang, 2006).

While sudden gains have proven to be an interesting avenue for prognostic research as well as research uncovering mechanisms of change, several criticisms to the initial account proposed by Tang and DeRubeis (1999) have been made. Firstly, studies have failed to replicate the finding that cognitive change precedes sudden gains (e.g. Hofmann, Schulz, Meuret, Moscovitch, & Suvak, 2006), though it remains a possibility that this is due to the reliance on session by session self-report measures as well as the failure to account for the temporal precedence of cognitive change relative to the occurrence of sudden gains. Differences in the definition of sudden gains (Shalom & Aderka, 2020; Vittengl, Clark, Thase, & Jarrett, 2015) also complicate the comparability between studies investigating mechanisms associated with sudden gains. More concerning, simulation studies cast doubt on the validity of sudden gains, especially in light of the fact that researchers identify them by exploring session-to-session change, usually across an average of 15 ($SD = 5$) sessions (see Shalom & Aderka, 2020). The evaluation of the absolute and relative magnitude of symptom change, as well as its stability, involves a researcher in multiple comparisons. Vittengl et al. (2015) conducted simulations to characterize the occurrence of sudden gains¹ by chance in datasets where the data-generating mechanism included sudden gains vs. linear change vs. log-linear change vs. no change. The results of that study suggested that sudden gains can occur by chance, even in datasets that were supposed to be

¹ Three different sets criteria and varying numbers of repeated measurements were used in this study.

characterized by the absence of change. Surprisingly, false-positive sudden gains occurred at a frequency high enough to be comparable to the occurrence rate of sudden gains in published studies (Median = 43%; Range = 5% to 76%). Other simulation studies have suggested that sudden gains may appear to happen even when the underlying data-generating pattern is one of gradual change (Thomas & Persons, 2013). Further concerns about the validity of sudden gains have been raised, including the fact that they may occur in placebo groups and pharmacotherapy (Vittengl, Clark, & Jarrett, 2005).

What is needed, then, is a way to test whether the occurrence of sudden gains, as well as their association with outcomes, happen above and beyond chance. In statistics, a randomization or permutation test can be used to obtain a distribution of potential values for a statistical test, and thus a p-value, for many different types of analyses (Ludbrook & Dudley, 1998). In the permutation test, the values on variables of interest are permuted (i.e., shuffled) on a random basis. Researchers then conduct the test statistic of interest across a large number of resamples (e.g., calculating the prevalence rate of sudden gains in a sample). From these analyses, one obtains a distribution of the test statistic obtained in the previous step from which a p-value can be calculated by determining how many of the random permutations have values that were below the statistic of interest. For example, suppose one had a sample of outpatients in which 30% of people were identified as having experienced a sudden gain. If across 10,000 permutations, values as high as 30% were found in 5,000 random re-samples, then $p = 0.50$ (5,000/10,000) and one would conclude that sudden gains were occurring at chance level. The logic of the permutation test is that if the null hypothesis is true, in this case that sudden gains are not occurring more than would be expected by error, then the data from the observed samples are 'exchangeable' or 'permutable' hence the name for this type of test. Permutations tests have been

used across a broad range of areas, including model-selection (Lindgren, Hansen, Karcher, Sjöström, & Eriksson, 1996), evaluating the performance of predictive models (Ojala & Garriga, 2010), and analyzing data from neuroimaging studies (Nichols & Holmes, 2002). An advantage of permutation tests is that they do not have many assumptions (LaFleur & Greevy, 2009; Welch, 1990), though a disadvantage is that they can be computationally intensive to conduct.

We propose that permutation tests may be a way of determining whether sudden gains occur in a sample above and beyond chance as well as determining whether the association between sudden gains and treatment outcomes occurs beyond chance-level. We explored the influence of randomizing weekly depression scores that are used to identify sudden gains within sessions (i.e., between participants) in a sample of patients in which sudden gains were previously identified (Lemmens et al., 2016). In this study, Lemmens et al. (2016) reported that in 117 patients randomized to CBT or IPT, sudden gains were associated with superior end of treatment outcomes in both treatments, though they were somewhat more likely to happen in CBT (42.2%, $n = 27$) than in IPT (24.5%, $n = 13$). We expect that sudden gains will occur in permuted data but they will be substantially less frequent and that the established association between sudden gains and treatment outcome is lost in the permuted datasets.

Method

Data source

The sample consisted of 151 adult outpatients, of which 117 provided usable data for the current analyses (see Data Preparation below). Participants were of the ages 18-65 and had enrolled in a randomized controlled trial examining the effectiveness of individual CT ($n = 76$) and interpersonal therapy (IPT; $n = 75$) for depression (Lemmens et al., 2011). They were eligible if they had a primary diagnosis of major depressive disorder (MDD), as determined by

the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First, Gibbon, Spitzer, Williams, & Benjamin, 1997). Participants were excluded if they were currently taking antidepressants, if the duration of their episode was over 5 years, or if they met criteria for a bipolar or substance use disorder or intellectual disability ($IQ < 80$). All participants provided written informed consent before entering the study, which was approved by the Medical Ethics Committee of Maastricht University approved the study protocol. The study is registered at the Dutch Cochrane Centre through the Netherlands Trial Registry (ISRCTN67561918).

Treatment consisted of 16-20 individual sessions, each lasting 45 min. CT was provided according to a protocol by (Beck, Rush, Shaw, & Emery, 1979). The IPT protocol was based on Klerman, Weissman, Rounsaville, and Chevron's (1984) manual. The primary outcome measure, the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996), was completed by patients immediately prior to each therapy session, at the end of the treatment phase (7 months), and monthly throughout the 5 month follow-up period (8–12 months). Further details have been published elsewhere (Lemmens et al., 2015, 2011).

Data preparation

We followed the methods of Lemmens et al. (2016), who analyzed their data as in Tang and DeRubeis (1999). That is, we included only those patients who received 8 or more sessions of therapy and whose BDI-II score at the first session was available, and was 15 or higher. Of the 76 CT patients, 12 were excluded (6 received fewer than 8 sessions, 2 had BDI-II scores that were missing, and 5 had BDI-II scores that were lower than 15 at the first session). In the IPT group, 23 out of 75 patients were excluded (9 received fewer than 8 sessions, 4 had missing BDI-II scores, and 10 had a first-session BDI-II score lower than 15). As some patients were excluded

for more than one reason, this resulted in sample sizes of 64 in the CT condition and 53 in the IPT condition.

Patients in this sample ranged in age from 18 to 63 ($M = 41.8$, $SD = 12.1$). Two-thirds (66.7%) were female, 59.8% were educated at an intermediate vocational level or higher, two thirds (60.7%) were married or in a committed relationship. The average score on the BDI-II at baseline was 30.6 ($SD = 8.5$) with more than half of the patients (58.1%) meeting the cut-off for severe depression on the BDI-II (BDI-II score ≥ 29 ; Beck et al., 1996).

Data analyses

All analyses were done using R (Version 4.0.0; R Core Team, 2020) in RStudio (RStudio Team, 2020) and made considerable use of packages from the *tidyverse* (Version 1.3.0; Wickham et al., 2019) for structuring and visualizing data. The analysis code for this study is available at <https://osf.io/d7rg2/>.

Sudden gains in the original dataset were identified following the three criteria outlined by Tang & DeRubeis (1999): (1) large absolute improvement of at least 7 points on the BDI-II, (2) large relative improvement of at least 25% of the pregain session score, and (3) large relative to symptom fluctuations. More details are reported in Lemmens et al. (2016). First, we provide descriptive statistics, mean (M) standard deviations (SD), and ranges, for depression severity at the beginning and end of the trial, overall and by sudden gain status.

Permutation test

To conduct permutation tests, 10,000 datasets were created from the current sample. BDI scores were permuted (i.e., randomized) within each session (i.e., between participants), see Figure 1 for three example trajectories of participants in the original data and permuted data. The permutations make it so that the average levels of depression at each session were identical in the

real and permuted datasets as were the standard deviations of scores. However, we expect that the session to session pattern is random (i.e., there is no autocorrelation between symptoms).

The R package *suddengains* (Version 0.4.4; Wiedemann, Thew, Stott, & Ehlers, 2020) was used to identify sudden gains in these 10,000 permuted datasets using the same criteria that were used to identify sudden gains in the original study (Lemmens et al., 2016). Next, we present the distribution of the frequency of sudden gains that were identified in the 10,000 ranpermutation datasets and conduct a permutation test comparing this distribution to the number of gains that were identified in the original study ($n = 52$). The p -value in these analyses is equivalent to the number of samples in the 10,000 permutations that had values equal or lower to the occurrence of sudden gains in the sample. In the original publication from these data by Lemmens et al. (2016), the authors reported that sudden gains were more likely to occur in CT than IPT. Thus, we conduct these permutation tests in the full sample as well as in each treatment condition.

Next, we focus on the association between sudden gains and outcomes. Here, too we conduct permutation tests within session (i.e., between participants). Randomizing within-session, sudden gains that are identified in the permutations should be unrelated to outcomes. Finally, we also conduct a permutation test where we randomize sudden gain status itself, which is another way of testing the association between sudden gains and outcomes.

Results

The average patient entered the trial with moderate-severe depression ($M = 30.6$, $SD = 8.5$) and exited the trial with lower depression scores ($M = 15.9$, $SD = 11.9$). In the original data, participants with sudden gains showed better treatment outcomes than participants without sudden gains (see Lemmens et al., 2016). Descriptive statistics for the frequency and outcomes

of sudden gains in the original and permuted datasets can be found in Table 1. Applying the sudden gains criteria to the permuted datasets confirmed prior findings: sudden gains could occur due to random chance with the average dataset having 29.43 ($SD = 5.01$) sudden gains across an average of 27.31 participants ($SD = 4.46$), or 23% of patients.

Identification of sudden gains

When permuting weekly depression scores of participants within each treatment session before identifying sudden gains, the mode of gains that were identified in 10,000 permutations was 29, which was only 55.7% of the frequency real data (i.e., 52; see Figure 2). In fact, no permuted dataset yielded a frequency as large as the one observed in the real data. Thus, the permutation test thus suggests that the frequency of sudden gains observed was unlikely to occur by chance ($p < 0.001$; $1/10,000$). In CBT ($p < 0.001$), the number of sudden gains was greater than what would be expected by chance but this was not the case in IPT ($p = 0.17$).

Sudden gains and treatment outcome

In the prior publication, Lemmens et al (2016) identified that having a sudden gain was associated with better outcomes on the BDI. In both of the approaches to permuting the data (i.e., randomizing sudden gains status and randomizing weekly depression scores), this association was lost (see Figure 3). Thus, these two permutation tests suggest that the association between sudden gains and outcomes that is observed in these data is very unlikely to occur under the null hypothesis that sudden gains are unrelated to outcomes ($p < 0.001$), see Figure 3A and 3B.

Discussion

We sought to determine whether a permutation test could be used for a significance test of the frequency with which sudden gains occur in a dataset as well for a significance test

probing their association with treatment outcomes. In a dataset in which sudden gains were previously reported to be present in over a third of the sample, and to predict superior acute treatment outcomes, we found that sudden gains could occur spuriously and did so on average for approximately 23% of patients in 10,000 permuted datasets. However, a magnitude as large as the occurrence in the full dataset was not observed in any permuted datasets, see Figure 2. Moreover, the association between sudden gains and acute outcomes in the datasets in which weekly depression scores or sudden gain status were permuted were very small and not statistically significant. We found evidence that sudden gains occurred above and beyond chance level in CBT but could not reject the null hypothesis that sudden gains occur by chance in IPT. We propose researchers utilize the permutation test to establish the statistical significance of sudden gains.

Limitations and strengths

Several limitations should be considered before interpreting our findings. First, we only conducted analyses in a sample of outpatients undergoing treatment for depression. Second, the permutation test analysis can be time-intensive. With the current dataset which had 117 observations across 20 sessions, we reported a runtime of over 30 hours². Finally, we employed the original sudden gain criteria by Tang & DeRubeis (1999), as opposed to developing statistical simulations to explore the effects of utilizing alternate criteria on the likelihood of detecting sudden gains. Notwithstanding these limitations, we made a novel contribution to the literature by proposing what is, to our knowledge, the first statistical test for the frequency of sudden gains. We studied sudden gains in a trial that is larger than most depression studies

² Analyses were run on a computer with a 2.6 GHz 6-Core Intel i7 processor and 16 GB memory.

(Barth et al., 2013). Finally, we provide the code to our analyses (<https://osf.io/d7rg2/>) to facilitate replications and further developments by other researchers.

Implications

Sudden gains and other studies of idiographic patterns of change may help reveal mechanisms of change in therapy (Hayes et al., 2007). Prior work, including statistical simulations, has raised the question of whether sudden gains occur even when the data-generating process is known to be linear, suggesting it may occur by chance (Thomas & Persons, 2013; Vittengl et al., 2015). Our analyses argue against this interpretation, at least in the current dataset. We should note that our findings should not be taken to imply that the number of gains produced in the permuted dataset should be subtracted from the total number of gains in the actual dataset or somehow used as a marker for how many gains in the dataset are “real” gains and which are not. The permutations suggest that, when the original data in this study ($n = 117$, 16-20 sessions) are randomized and an analysis of sudden gains occurs, in 95% of the permutation samples anywhere from 15-40 of gains will be present. The frequency we find is substantially greater than that. Nonetheless, the data-generating pattern is not random and likely differs between individuals. Additionally, the evidence to suggest that sudden gains occur above and beyond chance level was stronger for CBT than IPT. These results, together with the initial findings that the frequency of gains was higher in CBT than IPT (Lemmens et al., 2016), argue for the possibility that patterns of change, and possibly related mechanisms, differ between the two treatments.

We also conducted permutation tests where we randomized the session to session change pattern within each participant but retained their baseline and end of treatment score (see Supplement, Figure A2). Here, the difference between the raw and permuted dataset was larger

but these analyses may be a weaker test of whether sudden gains were occurring by chance because they only identify a small number of gains and only in the subset of people who had one large session-to-session change (i.e., who met sudden gain criterion 1). Future simulation work could explore whether these types of permutation tests are more appropriate to specific questions (e.g., on the association between gains and outcomes).

In our analysis, we found initial evidence that sudden gains occur above and beyond chance and in line with the results from Lemmens et al. (2016) that their association to treatment outcomes occurs above and beyond $p < 0.05$. We invite more researchers to use the permutation test in their samples when studying sudden gains. The use of more sophisticated methods to identify idiographic patterns of change in therapy could improve our understanding of individual differences and mechanisms in psychotherapy.

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Table 1

Descriptive statistics for sudden gains identified in the original data and permuted datasets

	Original data	Weekly depression scores permuted within sessions	
		<i>M (SD)</i> of SGs frequency	Range of SGs
Total sample (<i>n</i> = 117)			
Total number of SGs	52	29.43 (5.01)	[13, 47]
Participants with SGs	40	27.31 (4.46)	[12, 43]
CT (<i>n</i> = 64)			
Total number of SGs	35	15.75 (3.60)	[3, 29]
Participants with SGs	27	13.1 (3.09)	[3, 25]
IPT (<i>n</i> = 53)			
Total number of SGs	17	14.16 (3.48)	[3, 28]
Participants with SGs	13	13.1 (3.09)	[3, 25]

Note. CT = cognitive therapy, IPT = interpersonal therapy, SGs = sudden gains. *n* = number of participants.

Figure 1. Trajectories of depression symptoms for three participants with sudden gains in (A) the original data, (B) a dataset where BDI scores were permuted within sessions. Circles represent available data points and pregain sessions are highlighted as squares.

Figure 2. Total number of sudden gains in (A) the total sample, (B) the cognitive therapy (CT) condition, and (B) the interpersonal therapy (IPT) condition in 10,000 permuted datasets where weekly BDI scores were randomized within sessions. The solid grey line shows the mode of the distribution and the red dotted line shows the number of gains in original study for the total sample and each treatment condition.

Figure 3. Differences in treatment outcome on the BDI between all participants with ($n = 40$) and without ($n = 77$) sudden gains in 10,000 datasets with the following permuted variables: (A) Sudden gains status (B) session scores within sessions. The red dotted line shows the observed treatment difference in the original data. The average treatment outcomes for each group are shown in Figure A1.

Appendix

Data transparency statement

Previous publications with this dataset have explored the network dynamics of the BDI items (MS.11) as well as the short (MS.10) and long-term outcomes (MS.4) between the two treatments. Other papers have explored mediators (MS.7) as well as predictors of response in the acute phase of treatment (MS.1, MS.5-6, MS.9) as well as long-term (MS.2-3). In a previous manuscript (MS.8), our colleagues explored the frequency of sudden gains in CBT vs. IPT as well as the effect of sudden gains on outcomes. Here, we explore whether a permutation test can be used to determine whether sudden gains are occurring above and beyond chance-level.

Online Supplemental Material

Figure A1. Average BDI score at the end of treatment for participants with (green) and without (purple) sudden gains in 10,000 datasets with the following permuted variables: (A) Sudden gains status (B) session scores within sessions. Solid lines show the mean treatment difference found in the permuted datasets, dotted lines show the observed treatment difference in the original data. The treatment differences are shown in Figure 2.

Figure A2. Total number of sudden gains in the original data ($n = 52$) and the distribution of gains in 10,000 datasets where BDI scores were permuted within sessions. The solid grey line shows the mode of the distribution and the red dotted line shows the number of gains in the original study.