Chapter 5

The Self-Organization of Self-Injurious Behavior as Revealed through Temporal Pattern Analyses

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Abstract

Intentional acts of harm to self are among the most dramatic and disturbing behaviors exhibited by human beings and frequently exact a heavy toll in terms of the emotional and economic burden that must be borne by affected individuals, families, caregivers, and society. One major obstacle to understanding and treating self-injurious behavior (SIB) is the absence of adequate tools and methodologies to identify distinctive behavioral phenotypes or to quantify the complex presentation of SIB across varying time scales and environmental settings. Granted, there are increasingly sophisticated analytic techniques available to study behavior, but the vast majority of existing studies on SIB still rely on measures of frequencies or rates of SIB linked to a single environmental condition or other presumed contingencies. In contrast, our recent investigations of SIB among individuals with severe intellectual and developmental disabilities have employed temporal pattern analyses using the Theme™ program to explore the complex organizational dynamics underlying the presentation of SIB as recurrent patterns across time. Comprehensive behavioral and environmental events were recorded in situ, in real time, by trained, unobtrusive observers using The Observer®. The event codes and their associated times were then imported into Theme™, which was used to identify highly significant (i.e., nonrandom), recurrent, temporal patterns that were not constrained by implicit assumptions about the sequential ordering or hypothesized relations among the constituent events. Principal among our findings are that transitions to episodes of SIB are characterized by greater overall behavioral complexity and order within individuals; that self-injuring acts may serve as singular points that increase coherence within self-organizing patterns of behavior; that temporal patterns associated with SIB are highly correlated with basal beta-endorphin and adrenocorticotropic hormone levels across individuals; and that treatment with the opiate antagonist naltrexone may reduce the temporal patterning of SIB. The implication of these findings is that SIB can never be fully understood within a strictly linear conceptualization of "cause-and-effect" sequential dependencies. Instead, we suggest that SIB is dynamically regulated by "internal" processes which contribute to the emergence of complex, self-organizing patterns. If confirmed, these results may portend the development of innovative new behavioral or pharmacologic interventions designed to disrupt self-organizing regulatory processes, rather than simply focusing on putative antecedents or consequences.

Key words Self-injurious behavior, Self-organization, Temporal pattern analyses, Theme

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1 Introduction

Abnormality in human behavior is often characterized on the basis of functional criteria pertaining to whether the behavior is generally regarded as "adaptive" or "maladaptive" in a given social context or environmental setting. Behaviors that serve to increase productive or constructive adjustments to functioning in daily life are normally regarded as "adaptive," while behaviors that lead to impaired adjustments to functioning in a given social situation or setting are generally considered "maladaptive" in that they do not appear to serve a productive or constructive adjustment purpose. As such, maladaptive behaviors are thought to be counter-productive to the individual's own social, psychological, or physical well-being. Some of the most commonly observed maladaptive behaviors are repetitive, perseverative, or stereotyped movements, compulsions, tics, addictions, and intentional acts of physical harm to self.

Frequently termed "self-injurious behavior" (SIB), repetitive acts of self-harm are among the most dramatic and disturbing maladaptive behaviors exhibited by human beings. Although SIB has been observed in association with a variety of psychological disorders, neurological conditions, psychiatric diagnoses, and genetic syndromes, the primary focus of the investigations described herein is the frequent occurrence of SIB among individuals diagnosed with severe intellectual and developmental disabilities (IDD), including autistic spectrum disorders. The prevalence of SIB within this population has been estimated to be as high as 30 % and remains one of the primary reasons that individuals with IDD either are retained in institutional (restrictive) environments or administered psychotropic medication [1]. Despite considerable research effort, the underlying causes of SIB in this population remain a mystery and there is still no consensus among researchers and clinicians regarding the most effective interventions or treatments [2].

A major obstacle to understanding the mechanisms of SIB and developing coherent treatment plans has been an absence of reliable and effective methods for quantifying the complex, recurrent patterns of SIB across varying settings and time scales, such that relations with a variety of factors may be empirically assessed [3]. Indeed, the topographies and circumstances surrounding recurrences of SIB vary so considerably from one individual to the next that establishing a metric or analytical technique to reliably assess severity, change, or temporal contingencies is a major methodological impediment. Individuals exhibiting SIB employ an assortment of methods of self-harm that include cutting, hitting, or biting themselves, ingesting foreign objects, hurling themselves to the ground, and banging their head against solid objects often resulting in broken bones, disfigurement, blindness, or even loss of life [4–9]. This broad spectrum of self-harm phenotypes, the range of

methods used to commit these acts and the various motives proposed to explain them has militated against a unifying mechanism and the development of a universally effective intervention.

After considerable debate on this topic, a panel of experts convened by the US National Institute for Child Health and Human Development (NICHD) reached a consensus that it should be possible to define a distinct behavioral phenotype for SIB, perhaps with greater precision than most complex human behaviors because it is directly observable and can be reliably counted [10]. However, the NICHD group argued that data collection and analysis of SIB was primitive and that new methods of increasingly sophisticated sequential and temporal analysis of in situ observations of behavior were available [11–14] so that measures and analyses of patterns of SIB should replace or supplement measures of rate and frequency [4, 15]. Nonetheless, the majority of existing studies on this topic still rely on measures of frequencies or rates of SIB, often linked to a single environmental manipulation or experimental condition.

In contrast, our recent investigations of SIB among individuals with severe IDD have employed temporal pattern analyses using the Theme™ program [16, 17] to explore the complex organizational dynamics underlying the presentation of SIB as recurrent patterns across time. In conjunction with the application of temporal pattern analyses, our approach has also explored the heuristic utility of concepts derived from nonlinear dynamical systems theory to provide a unique perspective on the "internal" regulatory processes believed to subserve the persistent recurrence of SIB in this population. In so doing, it was hoped that this novel approach would catalyze the development and empirical testing of new hypotheses regarding the apparent self-organization of self-injurious and other maladaptive behaviors and eventually lead to innovative new treatment modalities for these troubling conditions.

2 Identifying Temporal Patterns of SIB

Increasingly sophisticated analytic techniques have been applied to the investigation of observationally recorded behavioral data over the past 30 years. For example, in 1979, Gene Sackett [13] described the application of lag sequential analyses to directly address the complexity and constraints of existing methods for identifying contingent relations across time in multivariate observational data. The conceptual basis for lag analyses derives from the quantitative methods of auto- and cross-correlation. When applied to qualitative behavioral data, the lag principle examines the conditional (or transitional) probability that a criterion event of interest will be sequentially followed by another event of interest (event lag), or that any observed event will fall within a specified temporal window in relation to the criterion event (time lag).

In the early 1990s, Eric Emerson and colleagues were among the first researchers to apply this analytic approach to the study of SIB among individuals with IDD. In a cross-validational comparison of time-based lag sequential analyses with traditional, experimental (functional) analyses, Emerson et al. [18] found a high degree of consistency between the two approaches (86 % agreement in the identification of behavioral processes underlying SIB). These results were interpreted as lending support to the external validity and overall viability of time-based lag analyses for exploring the mechanisms and contextual contingencies underlying SIB in IDD populations. Since then, several studies have applied this statistical method to quantify the conditional probabilities between recurrent acts of SIB and relations to a variety of other presumed behavioral and/or environmental antecedents or consequents.

Researchers from our project team have also employed time-based lag sequential analyses to examine whether successive episodes of SIB are sequentially dependent. In a study published by Marion et al. [19], sequential dependencies were determined by calculating the conditional probabilities that a match event followed a criterion event within four windows of time: 2, 10, 30, and 60 s. The results indicated that the only, highly significant, sequential predictor of SIB was another, antecedent occurrence of SIB. There was no evidence that SIB was sequentially dependent on environmental events or on other observationally recorded behaviors within these temporal windows. Furthermore, the method of analysis controlled for chance pairings of events and revealed that the sequential patterns of SIB were independent of frequency or rate of occurrence. Additionally, the conclusion that SIBs occur in sequentially related "bouts" was also confirmed using survival analyses to quantify the temporal distribution of SIB patterns [20]. The results reported by Kroeker et al. [20], suggested that, within some individuals with severe IDD, SIB followed "contagious" temporal distribution patterns, which could represent a unique behavioral phenotype that is maintained by biological rather than social or environmental factors.

Despite the meaningful application of lag sequential analyses in studies such as these, the method does have some inherent shortcomings that must be taken into consideration. For example, the temporal windows or variables of interest must be specified a priori. Implicit assumptions regarding the sequential or temporal proximity of contingent events, however, present serious limitations that may preclude the identification of "noncontiguous" or "long-range" temporal relations among events of interest. Furthermore, Sackett [13] cautions that lag sequential methods are highly vulnerable to "capitalization on chance," meaning that as the number of observations collected increases sufficiently, so too will the probabilities of finding significant sequential dependencies. While Bakeman and Gottman [21] provide detailed methods for controlling such

Type 1 errors, they caution that this is an issue of concern whenever lag sequential analytic methods are employed.

In the interest of overcoming such limitations in the study of SIB, our recent investigations [1, 3, 22] have utilized a unique, probabilistic, temporal pattern analysis program known as Theme™ (PatternVision Ltd and Noldus Information Technology BV). As developed by Magnusson [16, 17], Theme™ provides a statistical method of detecting temporal patterns (T-patterns) of related behavioral events that may not be obvious to a trained observer or identifiable by traditional or sequential analysis methods. The T-pattern detection algorithm first identifies significant (nonrandom) recurrences of any two events within a statistically similar temporal configuration (critical interval) in a real-time behavioral record and then proceeds to identify hierarchical relations with any other antecedent or subsequent events. Thus, the search algorithm detects highly significant, hierarchically arranged T-patterns that are composed of statistically related behavioral events that repeatedly appear in the same, relatively invariant, temporal configuration regardless of whether they are contiguous or noncontiguous in sequential distribution across time.

T-Patterns "grow" in complexity as simple patterns are incorporated into larger patterns, and are retained for further analysis according to whether they meet the search parameters specified by the user. Among these parameters is the probability that a given T-pattern will occur in a randomized distribution of the current record, the transitional probability that component patterns must possess to be included in a larger pattern, and the minimum number of instances that detected patterns recur across the record. Hence, the major advantages of this method are that it is not constrained by implicit assumptions about the sequential distribution of the behaviors of interest and allows the user to select the relevant probability levels to be tested against a randomized distribution of the actual behavioral record, thereby providing programmatic control over vulnerability to chance findings.

The following sections will provide a brief overview of the key findings that have been identified through the use of Theme™ in our analyses of observational data that were collected unobtrusively via handheld, mobile computers using The Observer® (Noldus Information Technology BV). For each of the studies detailed below, individual participants were observed by research staff throughout their regular daily routines, in situ, with minimal intrusion. The observation of individuals with varying self-injurious behavioral topographies required a coding strategy with a broad selection of the most salient features observed in the field and informed by previous research conducted over the past 30 years by Curt Sandman and colleagues at the University of California, Irvine. Though not described herein, details regarding the specific coding schemes employed, the reliability of the

observational procedures utilized, and the neuropeptide assay methodologies mentioned below can all be reviewed in previous publications from Sandman and colleagues [1, 3, 5, 6, 8, 19, 20, 22–28]. Furthermore, it should be noted that the following studies were all conducted in compliance with the Declaration of Helsinki. Informed consent was obtained from conservators and/or guardians of all study participants. The methods of consent and data collection as well as the specific study protocols were all reviewed and approved by the ethics oversight committees of the University of California, Irvine (UCI Institutional Review Board) and the State of California (Committee for the Protection of Human Subjects).

3 Comparing Temporal Patterns in Records *With* and *Without* SIB

A primary question when evaluating the utility of temporal pattern analyses in our studies was whether the occurrence of SIB would have a discernible impact on the overall temporal organization of the observed events. To answer this question we took 10 days of observational records from 32 individuals (18 male, 14 female; mean age = 40 ± 13 years) known to display SIB and separated them into records with and without an observed SIB. These records were analyzed with Theme™ (Version 5) and the quantitative results (mean number of distinct T-patterns, mean number of T-pattern occurrences, mean length, and mean level) were then compared using Paired-Samples *t*-tests. As can be seen in Fig. 1, records that included SIB produced significantly more distinct T-patterns ($t_{31} = 2.33$, $p < 0.03$; Fig. 1a), more T-pattern occurrences ($t_{31} = 2.14$, $p < 0.04$; Fig. 1b), longer T-patterns ($t_{31} = 2.19$, $p < 0.04$; Fig. 1c), and more complex T-patterns ($t_{31} = 2.37$, $p < 0.03$; Fig. 1d) when compared with records from the same subjects without an observed SIB. Furthermore, these comparisons remained significant even after controlling for an increased opportunity of detecting T-patterns (i.e., more recorded events) in records that included SIB by removing all SIB and staff-interaction codes from the records prior to rerunning the analyses.

As reported by Sandman et al. [22], these results indicate that SIB may function as a "singularity" around which a complex temporal configuration of behavioral patterns becomes increasingly self-organized. For example, it is possible that the temporal patterning of behaviors associated with SIB reflects the dynamical influence of an internal regulatory mechanism that drives the overall system toward greater behavioral coherence and complex structural integrity. Indeed, the dynamical processes underlying transitions between periods of relative calm and the occurrence on an episode of SIB may reflect a system that is in a critical state

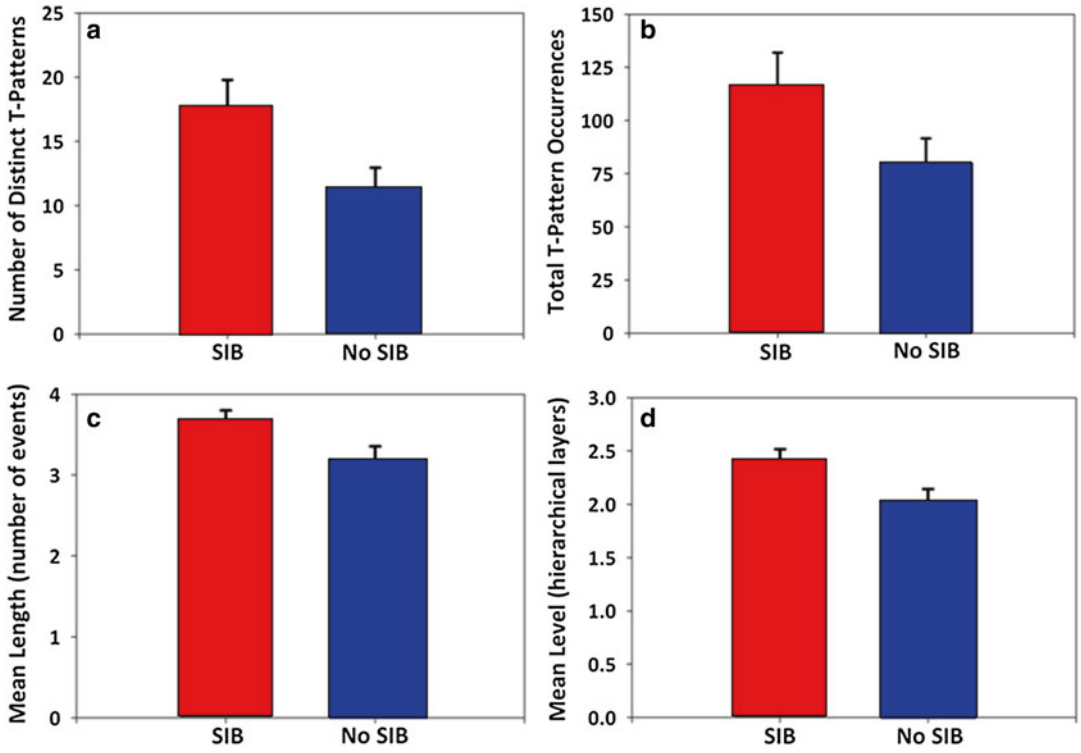

Fig. 1 Quantitative results of the temporal pattern (T-pattern) analyses on files with and without an observed episode of SIB. All of these mean values were found to be significantly different between files with and without an observed SIB episode on Paired *t*-test comparisons

at the "edge of chaos" [29], or some other process of self-organization [30]. Future research could serve to extend these results by investigating the specific mechanisms underlying the emergence of order that appears in the proximity of SIB (e.g., fractal patterns) [31].

Regardless of the specific mechanisms involved, however, transitions were observed between relatively disorganized behavioral states with few temporal patterns to a relatively organized state characterized by significantly more patterns, of greater complexity. It was surprising that the transition to a more organized state was observed when SIB was exhibited because increased complexity and system integrity typically are associated with "adaptive" states [32] and biopsychosocial resilience [33]. It is possible that the movement from behavioral calm to periods of self-inflicted injury confers an adaptive advantage or gain for the individual. For example, SIB could actually produce a movement toward equilibrium in biologically mediated processes associated with the regulation of arousal [34], reward, or pleasure [25], particularly if those processes are already in a state of dysregulation [26].

4 Exploring Relations between Temporal Patterns of SIB and Neuropeptides

Among the biological processes that have been suggested to contribute to the emergence and maintenance of SIB is the stress-related molecule proopiomelanocortin (POMC). Evidence from our laboratory, and several others, has indicated that the processing and release of POMC in the hypothalamic–pituitary–adrenal (HPA) axis may be perturbed among subgroups of individuals exhibiting SIB [1, 5, 6, 25–28, 35–55]. For example, Sandman et al. [25, 26] reported that sequentially dependent patterns of SIB reached highest conditional probabilities among individuals who exhibited a dysregulation, or "uncoupling," of the POMC system, as characterized by elevated basal levels of β-endorphin (βE) relative to basal levels of adrenocorticotropic hormone (ACTH). These two hormones are POMC-derived neuropeptides that are involved in the stress response as part of the HPA axis (ACTH), and in the modulation of pain and pleasure because of their affinity for the opiate receptors (βE).

Despite such evidence implicating the role of POMC, measures of rate or frequency of SIB have never been shown to have a direct correlation with blood levels of the POMC-derived hormones, βE and ACTH. As the sequentially dependent patterns of SIB revealed a significant (though indirect) association, we hypothesized that a more robust pattern detection method such as Theme™ could further elucidate the hypothesized relations between disturbed basal levels of βE and ACTH and a unique behavioral presentation of temporally patterned recurrences of SIB. Accordingly, we used Theme™ (Version 5) to identify T-patterns that included SIB within a dataset of in-situ observational recordings spanning 8 days (~40 h) in 25 individuals (13 male, 12 female; mean age = 40.5 years) with IDD and a history of persistent SIB for whom we also had basal (morning) blood levels of βE and ACTH.

As reported by Kemp et al. [3], and summarized in Table 1, the results of this investigation indicated that the within-subject percentages of detected T-patterns containing SIB were highly correlated with basal levels of βE ($r = 0.79$, $P < 0.001$) and ACTH ($r = 0.79$, $P < 0.001$). These correlations were even higher for the proportion of detected T-patterns that included both SIB and agitated behaviors (AB), but were not significant for the proportion of T-patterns containing AB without SIB or for any of the other "control" behaviors such as non-injurious motor stereotypies or staff interactions. Furthermore, such high correlations were not found, and have not been previously reported, between "raw" frequency counts or rates of SIB and these hormone levels. This indicates that the detection of temporally distributed patterns of SIB may yield measures more directly relevant to the underlying

Table 1
Pearson's *r* correlations (sig.) between hormone levels, behavior counts and rate (rows) and Theme results (columns), including total T-patterns and the proportion of T-patterns containing SIB, agitated behavior (AB), both SIB and AB, motor stereotypy (STER), and staff behaviors (STAFF)

	Total T-patterns	% SIB T-patterns	% AB T-patterns	% SIB and AB T-Patterns	% STER T-patterns	% STAFF T-patterns
βE level	0.29 (0.147)	**0.79 (<0.001)**	0.17 (0.403)	**0.83 (<0.001)**	−0.09 (0.668)	−0.06 (0.759)
ACTH level	0.23 (0.265)	**0.79 (<0.001)**	0.18 (0.371)	**0.85 (<0.001)**	−0.14 (0.494)	−0.09 (0.660)
Total SIB	0.08 (0.690)	0.20 (0.337)	0.06 (0.755)	0.15 (0.481)	0.22 (0.228)	0.04 (0.839)
SIB per hour	0.12 (0.585)	0.22 (0.274)	0.06 (0.748)	0.17 (0.401)	0.21 (0.243)	0.03 (0.892)
Total behaviors	**0.57 (0.003)**	0.37 (0.073)	−0.23 (0.270)	0.29 (0.163)	**0.44 (0.011)**	−0.26 (0.213)

biological mechanisms than traditional methods of quantifying occurrences. Furthermore, these results suggest the potential utility of temporal pattern analyses to identify a sub-type of subjects that may respond most beneficially to certain treatment approaches (e.g., opiate antagonists).

5 Examining the Effects of Naltrexone on Temporal Patterns of SIB

In the early 1980s, Sandman and colleagues were among the first to present evidence that opiate antagonists could be used to reduce the occurrences or attenuate the severity of SIB among individuals with IDD [46]. Since then numerous studies have explored the putative efficacy of opiate antagonists (e.g., naltrexone or naloxone) for the treatment of SIB. Although there have been some reports that have not shown clear support for the efficacy of this intervention [56], several reviews of this approach [1, 57–59] have reported improvements ranging from 57 to 80 % across numerous studies of individuals treated with naltrexone, with "unequivocal responders" comprising from 25 to 47 % of cases reviewed. One of the outcomes of research on this topic has been the suggestion that there may indeed be subgroups of individuals that respond most favorably to treatment with opiate antagonists. Furthermore, as noted above, one of the obstacles in identifying possible biological indicators of treatment responsiveness has been the reliance on relatively simple methods of analysis (e.g., rate or frequency of occurrence) that do not capture the complex expression of SIB as patterns across time.

In order to evaluate whether temporal patterns of SIB may provide a more sensitive measure of the effects of opiate antagonists, we conducted a small study in which six individuals (four male, two female; mean age = 38 years) with IDD and a persistent history of SIB were administered three dose levels of naltrexone (0.5, 1, and 2 mg/kg) for 1 week each, with intervening weeks receiving placebo, and the ordering of doses counterbalanced across subjects. Observational recordings were analyzed separately for each week using Theme™ (Version 5) and the results were then aggregated to compare the proportion of T-patterns containing SIB with the proportion of SIB events in the overall behavior frequency counts observed during the baseline week, and the weeks during which the subjects received either a placebo or one of the three doses of naltrexone. The results of these comparisons are shown in Fig. 2.

These results clearly indicate that SIB T-patterns provide a more sensitive measure of the effects of naltrexone, despite the fact that the small sample size precluded statistical significance for these comparisons. With regard to "clinical significance," one could argue that a reduction of SIB T-patterns would be relatively meaningless if the frequency of SIB shows no changes. However, an alternative interpretation is that the effects of naltrexone may serve to disrupt the underlying biological processes that subserve the organization of SIB into patterns, as expressed across time, thereby creating a condition which could make SIB more amenable to behavioral interventions.

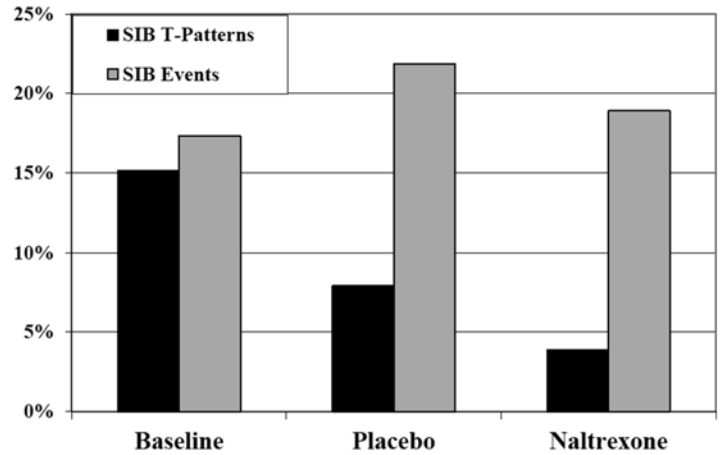

Fig. 2 Mean percentages of SIB T-patterns (out of total detected T-patterns) and SIB Events (out of total recorded behavioral events) detected during Baseline week and during weeks that the subjects were receiving either placebo or naltrexone treatments

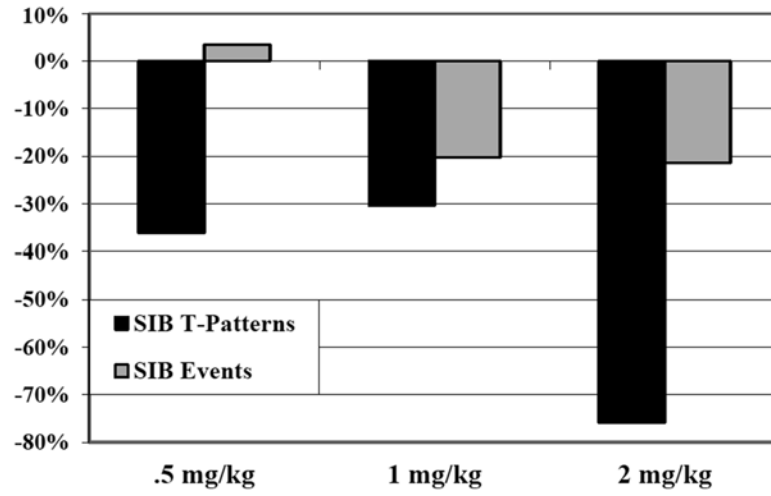

Fig. 3 Mean percentage decreases from placebo to respective naltrexone dose levels for the percent of T-patterns containing SIB (out of total detected T-patterns) and the percent of SIB events (out of total recorded behavioral events). These changes are matched for each subject for the weeks immediately preceding each dose of naltrexone

With regard to the apparent "placebo effect" seen in the change from baseline for the SIB T-patterns in Fig. 2, it should be noted that the dosing of placebo and naltrexone was counterbalanced across subjects on alternating weeks. Accordingly, the aggregation of respective placebo and naltrexone weeks includes potential "carryover" effects from a previous dose of naltrexone. This is more likely to be the reason for the decrease from baseline levels than the "expectation" bias commonly associated with an actual placebo response. Alternatively, Fig. 3 provides a comparison of SIB T-pattern and SIB event percentages that are matched for each subject to show the percent change from the placebo week immediately preceding each of the doses of naltrexone. Again, it appears clear that SIB T-patterns revealed a more pronounced effect in the percent change from weeks during which the subjects received placebo to the following weeks during which the subjects received the respective doses of naltrexone.

In addition to the observational data collected during this small trial, we also had blood levels of the N-terminal fragment of beta-endorphin (βEN) that were collected from each of these subjects prior to the initiation of the drug trial. Samples were collected within 2–5 min after an episode of SIB (defined as the observation of at least one self-injurious act). Control samples were collected on separate days, following a period of at least 30 min without an episode of SIB, and were matched for time of day with the post-SIB samples. To further control for the possible influence of physical exertion, samples were also collected on a separate day following

Table 2
Pearson's *r* coefficients (significance) between levels of beta-endorphin (N-terminal) collected in either the A.M., P.M., or following SIB, no SIB, or physical exercise (PE) and the change in the percent of T-patterns (by behavior type) between weeks treated with placebo and naltrexone

Change in T-pattern % by behavior type	Beta-endorphin (N-terminal) levels				
	A.M.	P.M.	Post-SIB	No-SIB	Post-PE
SIB	0.37 (0.47)	0.25 (0.64)	**0.82 (0.045)**	–0.45 (0.44)	0.66 (0.22)
Stereotypy	–0.76 (0.07)	–0.26 (0.96)	0.52 (0.29)	–0.29 (0.64)	–0.10 (0.87)
Staff interactions	0.42 (0.41)	0.54 (0.27)	0.35 (0.49)	–0.63 (0.25)	0.26 (0.68)

a brisk 10-min walk (physical exercise). Finally, on a separate day from the other samples, morning (8 A.M.) and afternoon (4 P.M.) samples were collected (on the same day) to estimate the peak and nadir, respectively, of the peptide levels under investigation.

As shown in Table 2, these βEN levels were compared with the percentage change in T-patterns (by behavior type) from the weeks the subjects were treated with placebo to the following weeks in which they received naltrexone. Despite the small sample, a highly significant correlation was detected between post-SIB levels of βEN and the change from placebo in the percentage of T-patterns containing SIB to the weeks subjects were receiving naltrexone. No such correlations were found for changes from placebo on any "control" T-patterns (i.e., those containing non-injurious, stereotyped behaviors or staff interactions). These findings suggest post-SIB βEN levels may have direct relevance to the effects of naltrexone on the temporal organization of SIB.

Though limited by a relatively small sample size, these findings may be the first to demonstrate a relation between response to a pharmacological intervention for SIB and endogenous levels of the N-terminal fragment of βE. At least one study [55] has suggested a relatively unrecognized role of the N-terminal in the processes thought to subserve SIB; however, there are no previous studies that have suggested that post-SIB levels may have direct relevance to whether an individual may respond favorably to treatment with naltrexone. Such relations may portend a more complete understanding of the biological mechanisms underlying the persistent and disturbing recurrence of SIB among certain individuals with developmental disorders and clearly warrant further investigations. Without the utilization of temporal pattern analyses in these investigations, however, such relations might continue to lie unrecognized, as traditional linear analyses may not possess adequate sensitivity to reveal the complex emergent structuring of these behaviors across time.

6 Comparing Temporal Pattern Analysis with Lag Sequential Analysis

The studies described above have undoubtedly demonstrated the utility of temporal pattern analyses in the investigation of SIB. Nonetheless, we have also sought to evaluate the relative merits of this method in a direct comparison with the other method of analysis that has been extensively applied in the study of observational data: lag sequential analysis. As noted earlier in this chapter, researchers from our laboratory have applied lag sequential analyses on a number of studies, but were uncertain as to how those findings might have differed if temporal pattern analyses had been applied instead. Accordingly, we conducted a direct comparison of these two complementary methods and examined how they differ with regards to the type of information each may yield when applied to the study of SIB. Furthermore, this study also provided an opportunity to compare the sensitivity of each method to diurnal levels of a stress-related hormone (cortisol) and their respective utility for detecting changes associated with acute and long-term treatment with naltrexone in a case study of a single subject.

This case study included 74, 2-h, observational records collected via unobtrusive, in situ observation of an 11-year-old boy diagnosed with autism and a persistent history of severe SIB. These observational records were collected during three separate time periods, each spanning approximately 1 month, with approximately 6 months between each period. The subject was not receiving any medications during the first observational period and began taking a daily dose of 2 mg/kg of naltrexone 2 weeks into the second period and continued taking this dose throughout the remaining time periods. As such, the "acute" effects of naltrexone described below were evaluated within the second time period, whereas the "long-term" effects were evaluated using data from the third time period. During the third time period, salivary cortisol samples were also collected for 21 consecutive days at four daily time-points: 6:30, 7:00, and 7:30 A.M. to detect the cortisol awakening response, and at 4:00 P.M. to measure the approximate nadir.

All 74 observational records were analyzed using both lag sequential and temporal pattern analyses. Lag sequential analyses were conducted using The Observer® XT (Version 9) to calculate event-based conditional probabilities across all recorded categories. The comparisons described below included the conditional probability of an SIB event contiguously following another SIB event, as this measure previously had been found to be highly sensitive to the treatment effects of naltrexone and to biological variables of interest [25, 26]. Temporal pattern analyses were conducted with Theme™ (Version 5) using the following search parameters: Minimum Occurrence of 3, Significance Level less than 0.05, and a Lumping Factor of 0.99, with all other parameters set to default values.

The conditional probabilities that an SIB event would be followed by a subsequent SIB event (SIB-SIB CPs), as calculated using lag sequential analyses, was found to be significantly correlated with the total number of T-patterns detected by Theme™ ($r = 0.44$; $p < 0.001$), the number of T-patterns containing SIB ($r = 0.32$; $p < 0.005$), and the proportion of T-patterns that contained an SIB event ($r = 0.63$; $p < 0.001$). The raw frequency counts of SIB were also found to be highly correlated with SIB-SIB CPs ($r = 0.70$; $p < 0.001$), the total number of T-patterns ($r = 0.64$; $p < 0.001$), the number of T-patterns containing SIB ($r = 0.56$; $p < 0.001$), and the proportion of T-patterns that contained an SIB event ($r = 0.59$; $p < 0.001$). This indicates that these measures are highly related and share ~9 to ~40 % common variance. What a direct correlational comparison does not address, however, is whether there are differences in the types of information that can be derived from each method. To address this issue, we also examined the sensitivity of each method to diurnal cortisol levels and their relative utility for detecting changes associated with acute and long-term effects of naltrexone.

Table 3 provides a comparison of how well SIB frequency counts, SIB-SIB CPs, and SIB T-patterns correlated with salivary cortisol levels. All three measures showed modest, though nonsignificant, trends for inverse correlations with the A.M. cortisol levels. For the 4:00 P.M. samples, however, elevated levels of cortisol were significantly associated with the number of T-patterns that included SIB ($r = 0.61$; $p < 0.005$). Correlations between afternoon cortisol levels and SIB frequency counts were also positive but only marginally significant, while SIB-SIB CPs showed no relations at all with this measure. Finally, the largest correlations with cortisol were for the percent decrease from A.M. to P.M. levels. Significant negative correlations with this measure were found for both SIB frequencies ($r = -0.57$; $p < 0.01$) and SIB T-patterns ($r = -0.81$; $p < 0.001$), but not for SIB-SIB CPs, indicating that days with flatter diurnal variation were associated with a greater probability of

Table 3
Pearson's correlation coefficients (significance) for comparisons between salivary cortisol levels and various measures of SIB

	SIB frequency	SIB-SIB CPs	SIB T-patterns
Cortisol—6:30 A.M.	−0.27 (0.29)	−0.19 (0.44)	−0.28 (0.26)
Cortisol—7:00 A.M.	−0.26 (0.29)	−0.22 (0.38)	−0.35 (0.15)
Cortisol—7:30 A.M.	−0.28 (0.26)	−0.26 (0.29)	−0.43 (0.08)
Cortisol—4:00 P.M.	0.43 (0.06)	0.00 (0.99)	**0.61 (0.005)**
% Decrease A.M.–P.M.	**−0.57 (0.01)**	−0.02 (0.92)	**−0.81 (0.0005)**

Table 4
ANOVA results comparing the changes in three measures of self-injurious behavior (SIB) following treatment with naltrexone for 3 weeks (acute) and 6 months (long-term)

	Baseline	Acute effects		Long-term effects	
	Mean (SD)	Mean (SD)	*F*-value (sig.)	Mean (SD)	*F*-value (sig.)
SIB T-patterns (%)	55.8 (16.2)	30.4 (23.5)	**5.61 (0.03)**	13.6 (25.2)	**15.59 (0.0005)**
SIB-SIB CPs	0.04 (0.01)	0.04 (0.02)	0.25 (0.62)	0.02 (0.02)	**12.54 (0.001)**
SIB frequency	55.0 (51.9)	26.4 (18.4)	3.05 (0.10)	8.3 (12.9)	**24.13 (0.0005)**

SIB and SIB T-patterns. This would appear to indicate that this subject's cortisol levels remained unusually high well into the afternoon on days when SIB occurred at higher levels and a high proportion of his temporally organized behavioral patterns included SIB among their constituent events, regardless of SIB-SIB sequential dependencies. Overall, these findings indicate that temporal pattern analyses offer superior sensitivity to this biological measure and merit further application in future investigations into the possible contributory role of disturbed diurnal patterns of cortisol in relation to the temporal patterning of SIB.

Table 4 provides a summary of the differential sensitivity of these measures to changes associated with the administration of naltrexone. Repeated-measures ANOVA comparisons revealed that the proportion of T-patterns containing SIB decreased significantly ($F = 5.61$; $p < 0.03$) in the weeks immediately following the initiation of naltrexone. By contrast, no significant acute changes were seen in SIB-SIB CPs or in the raw frequency counts of SIB, though the latter did show a sizable decrease. The repeated-measures ANOVA comparisons of the "long-term" effects, following 6 months of treatment with naltrexone, however, revealed highly significant decreases in all three of these measures: the proportion of T-patterns containing SIB ($F = 15.59$; $p < 0.001$), SIB-SIB CPs ($F = 12.54$; $p < 0.001$), as well as the raw frequency count of SIB events ($F = 24.13$; $p < 0.001$).

Of note, the proportion of T-patterns containing SIB was the only measure to show a statistically significant change during the first few weeks of treatment. Although SIB frequency counts also decreased by more than 50 % this change was not found to be statistically significant. This may mean that SIB T-pattern percentages could yield important predictive information with regards to intervention effectiveness, even when clinically observable effects could be masked by the higher variability in raw frequency counts. The clinical implications of this finding are that physicians may prematurely decide to discontinue treatment with naltrexone on the basis that no notable effects on SIB are observed by the caregivers within

the first few weeks. However, these findings would suggest that such a decision, made on the basis of subjective impressions or SIB frequency counts alone, may discount the possibility that naltrexone may produce "subclinical" acute effects on processes subserving SIB, which may only be observable with more sophisticated analytic methods. As suggested earlier in the chapter, naltrexone may serve to disrupt the underlying temporal organization of emergent SIB patterns by blocking the contributory role of the endogenous opiate β-endorphin, thereby creating a condition which could potentiate the success of other behavioral interventions.

7 Examining the Self-Organization of SIB Dynamics

As described by Pincus et al. [60], self-organizing systems are essentially systems in nature that exhibit emergent order through the interactions of sufficiently complex coupling relationships among interacting components. Once such a system emerges, it is maintained over time through reciprocal feedback from the global level back down to the parts, leading to subsequent emergence over time. Self-organization is considered adaptive within "living" systems (e.g., biological, behavioral, or social systems) because it allows such systems to adjust their levels of structural organization towards rigidity or flexibility depending upon environmental demands. Numerous examples of self-organization exist in nature, such as flocking behaviors (e.g., migratory birds, humans in a crosswalk, or driving in traffic), collective survival behaviors (e.g., swarming insects or ant colonies), and also across the various domains of psychological science [61] including: small group dynamics [62], psychotherapy processes [63], emotional dynamics [64], and symptom covariations underlying psychopathology [65].

In the interest of examining whether temporal patterns of SIB displayed the hallmark characteristics of self-organization, Pincus et al. [60] utilized orbital decomposition (OD) [66, 67] to analyze the observational data collected by Sandman et al. [22] and described earlier in this chapter. OD is a technique based on symbolic dynamics designed to identify patterns and measure complexity within categorical time-series data. The use of OD provided a means to test the role of SIB within self-organizing behavior–environment pattern dynamics by producing several theoretically grounded measures of systemic complexity (i.e., Shannon entropy, topological entropy, Lyapunov dimension, and fractal dimension), essentially measures of order and disorder. These entropy measures allow one to empirically examine self-organization in behavioral flows and allowed us to compare the results of this method of analysis with those obtained using Theme™.

The results of this analysis revealed that the dynamics observed in these data were generally what would be described as low dimensional

chaos or "edge of chaos" dynamics as described by Kauffman [68] and others as hallmarks of self-organization. This conclusion is based on the Lyapunov dimension value between 1 and 2 (mean $D_l = 1.2$), the fractal dimension between 2 and 3 (mean $D_f = 2.542$), and strong fits to inverse power-law distributions (mean IPL $R^2 = .93$). These results strongly suggest that the behavior-environment dynamics described in the Sandman et al. [22] study would be accurately characterized as self-organizing behavioral flows.

Furthermore, a comparison of records with and without SIB also revealed that the series with SIB contained significantly longer deterministic patterns (mean SIB = 12.48, mean No-SIB = 8.47; $p = 0.008$; $t = 2.658$), a higher number of behaviors within the same time-period (mean SIB = 173, mean No-SIB = 134; $p < 0.001$; $t = 3.702$), and a greater observed variety of behavioral codes (mean SIB = 10.70, mean No-SIB = 9.47; $p = 0.001$; $t = 3.404$). Altogether, longer patterns, higher activity, and higher variety culminated in higher levels of Shannon entropy in series containing SIB (mean SIB = 4.61, mean non-SIB = 4.36; $p < 0.001$; $t = 3.642$). It appears that SIB promotes more behavioral shifting, variety, and unpredictability of patterns. These results suggest that series containing SIB are more coherent (i.e., pattern length), yet also more complex (i.e., higher Shannon entropy), which is consistent with the results reported by Sandman et al. [22] using Theme™ to quantify the temporal patterning of SIB.

8 Theoretical Implications and Future Directions

Theories regarding the persistent recurrence of SIB among individuals with IDD have generally embraced either a strict behavioral or biological perspective. The behavioral account proposes that SIB is reinforced through operant conditioning [69], for example as a means of escaping demands [70, 71], relieving anxiety or seeking attention [34]. Indeed, a number of studies have shown positive outcomes for behavioral interventions which lend support to this conditioning perspective [72, 73]. The biological perspective focuses on physiological and neurological processes associated with SIB, and considers its recurrence in relation to the endogenous release of opiates or other disturbances in the pain, pleasure, or arousal centers of the brain [1, 59]. Treatments aimed at blocking pleasure receptors, lowering pain thresholds, and decreasing arousal have also proven effective in a number of studies [57–59]. Nevertheless, no clear consensus has emerged from either line of investigation and there are no universally effective treatments.

In our recent investigations, described above, we have utilized a sophisticated method of time-pattern analysis (Theme™) and explored the utility of concepts derived from nonlinear dynamical systems theory. It was hoped that this novel approach would provide

new insights into the mechanisms subserving the persistent recurrence of SIB, instigate the formulation of new hypotheses for future empirical studies, and eventually lead to the development of innovative new treatments. Indeed, the findings reported herein do support the perspective that the temporal patterning of SIB is an overt expression of a self-organizing process that defies classical interpretation from either a prevailing behavioral or biological viewpoint. Perhaps it is time for researchers of SIB to begin exploring new nosological concepts that are not constrained by traditional theoretical frameworks.

Commonly referred to as "Chaos Theory," the dynamical systems perspective has been growing in popularity over the past 25 years thanks in large part to best-selling books such as *Chaos: Making a New Science* by James Gleick [74] and *At Home in the Universe* by Stuart Kauffman [68]. Among the more important recent developments, is the work of Per Bak, Chao Tang, and Kurt Wiesenfeld, who first introduced the concept of "self-organized criticality" [75]. As noted earlier, a self-organizing dynamical system is one in which complex order can emerge through the interactions of lower-order components. The concept of "self-organized criticality" describes the property of some dynamical systems that are balanced at their critical point (i.e., at the "edge of chaos"), such that slight perturbations of the system can trigger large transitions, or the emergence of a complex rearrangement in the overall state of the system. The classic examples of this are a sand pile shifting under the weight of a few added grains of sand, or a massive avalanche being triggered by the added weight of a solitary skier. These systems can be described as having self-organizing, critical-state dynamics as they are poised at the edge of large transitions, whereby a small change in the system can lead to large-scale changes and greater emergent complexity.

Recent studies [76–79] have described "self-organized criticality" in the human brain, particularly in the critical balancing of inhibitory/excitatory projections within cortical–subcortical loop circuits through activity-dependent, dynamic modulation of synaptic receptor densities or other mechanisms of neural plasticity (e.g., long-term potentiation or depression). It has been suggested that these dynamic modulation processes serve to keep the summation of inhibitory and excitatory projections within these neural loop circuits poised at a critical state to maximize information processing capacity and maintain the flexibility of the system to rapidly respond to environmental demands or other changes in the condition of the overall system. The critical-state dynamics of this system include "long-range temporal correlations" that fluctuate with the amplitude envelopes of neuronal oscillations (e.g., electroencephalography), and "neuronal avalanches" which are spatiotemporal cascades of activity that emerge from the aggregation of local field potentials within parallel neural loop circuits.

Parallel "cortico-striatal-thalamo-cortical" loop circuits are believed to regulate the patterning, storage, and elicitation of complex behavioral repertoires, as well as various motoric, affective, and cognitive "control" processes, and have been shown to be disturbed in individuals with schizophrenia and autism [78–84]. These same cortico-striatal loop circuits have also been suggested as a key neurobiological mechanism involved in the generation and maintenance of repetitive "maladaptive" behaviors, such as motor stereotypies, compulsions, addictions, and even SIB [83, 84]. Furthermore, in addition to the well-known dopaminergic and GABAergic projections within these cortico-striatal loop circuits, recent evidence suggests opioid neuropeptides mediate communication between medium spiny striatal projection neurons which may "provide a new cellular substrate for competitive dynamics in the striatum" [85]. In fact, recent findings also suggest that "an intact endogenous opioid system is necessary for normal goal-directed learning and more importantly, reveal that a compromised endogenous opioid system during learning enhances the habitual control of actions" [86]. In short, these studies have implicated a relatively unrecognized role of opioidergic striatal projections in the dynamic modulation of neural loop circuits that are widely believed to subserve the learning and elicitation of complex behavioral sequences which may either be goal-directed ("adaptive") or habitualized ("maladaptive").

If these neural loop circuits do display "self-organized criticality," as has been suggested, then it would be reasonable to expect that the dynamics of this underlying system should be observable at a behavioral level, particularly since the critical-state dynamics of a self-organized system should be multilevel, self-similar, and scale-independent, by definition. As reported by Pincus et al. [60], and described above in this chapter, the temporal patterning of SIB within the observational records collected by Sandman et al. [22] do display the hallmark characteristics of a self-organized dynamical system poised in a critical state at the "edge of chaos." Accordingly, it is quite possible that the self-organization of self-injurious behavior, as revealed through temporal pattern analyses, could be regarded as an endophenotypic expression of systemic perturbation within the critical-state dynamics of the underlying cortico-striatal loop circuits of the human brain.

Granted, such suggestions are rather speculative; however, it is precisely this type of approach that will be required to overcome the limitations of traditional, linear, cause-and-effect, conceptualizations of complex behavioral phenomena like SIB, and begin to define new behavioral phenotypes with direct relevance to understanding the underlying neurobiological mechanisms. In 2009, the US National Institute of Mental Health (NIMH) launched its Research Domain Criteria (RDoC) project "to develop a research classification system for mental disorders based upon dimensions

of neurobiology and observable behavior" [87–89]. The basic premise of this approach is that existing diagnostic categories do not provide an adequate foundation for research into the possible neurobiological mechanisms underlying "abnormal" behavior, as expressed across a dimension of "normal" behaviors. From this perspective, research into the neurobiological mechanisms believed to subserve SIB must seek to quantify a dimension of behavioral processes that may be linked with discrete neural circuits which, when perturbed, result in the perpetuation of maladaptive patterns of behavior, with self-injury occurring at the extreme. As such, our results described herein are directly aligned with the RDoC approach recommended by the NIMH.

In addition to the possibility of providing a new theoretical framework for future investigations of SIB, the implications of the findings presented herein also raise many questions that additional studies might address: Are there common neurobiological mechanisms underlying the learning, expression, and temporal patterning of complex human behaviors across a dimension from normal to abnormal? Do these mechanisms display self-organizing, critical-state dynamics that could be quantified across multiple levels of investigation? What are the "tuning" parameters that could modulate the dynamics of this system? Could a "dysregulation" of the opioidergic system (or other biological process) perturb the critical-state dynamics within the neural loop circuits that are thought to regulate the storage and elicitation of behavioral patterns? Are there other processes that could be used to modulate the dynamics of these circuits?

Finally, we sincerely hope that the current findings and somewhat speculative discussion presented in this chapter will serve to catalyze the development of innovative new treatments for SIB, as well as other maladaptive behaviors. For example, there are several neuromodulatory techniques that offer the potential of directly "tuning" the processes implicated in the dysfunctional perpetuation of maladaptive behaviors. In our previous studies exploring the use of repetitive transcranial magnetic stimulation (rTMS) in the treatment of schizophrenia [90, 91], we demonstrated that the "resonant tuning" of intrinsic alpha-frequency stimulation could be used to increase the amplitude and selectivity of frontal alpha oscillations and produce clinically significant improvements in symptom severity. There are several investigators that are currently exploring the efficacy of rTMS in the treatment of individuals with autistic spectrum disorders. At present, there is at least one published report that offers a preliminary indication that this technique could be beneficially applied in the treatment of SIB, as evidenced by a significant reduction in repetitive behaviors following low-frequency rTMS [92]. Future studies should seek to provide a theoretical basis for the mechanism of action of such neuromodulatory techniques, and we believe that the current

chapter provides a viable framework for exploring the putative efficacy of such innovative new interventions for the treatment of SIB. Without the use of Theme™ to identify the dynamics underlying the temporal patterning of this complex and horribly debilitating behavior, however, the foundational tenets of our approach would likely remain unseen and undetected.

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