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Change point analysis for longitudinal physiological data: Detection of cardio-respiratory changes preceding panic attacks

David Rosenfield [a,*], Enlu Zhou [b], Frank H. Wilhelm [c], Ansgar Conrad [d], Walton T. Roth [c], Alicia E. Meuret [a,**]

[a] Department of Psychology, Southern Methodist University, 6424 Hilltop Lane, Dallas, TX 75275, USA
[b] Department of Industrial and Enterprise Systems Engineering, University of Illinois at Urbana-Champaign, USA
[c] Department of Psychology, University of Basel, Switzerland
[d] Department of Psychiatry and Behavioral Sciences, Stanford University, USA

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ABSTRACT

Statistical methods for detecting changes in longitudinal time series of psychophysiological data are limited. ANOVA and mixed models are not designed to detect the existence, timing, or duration of unknown changes in such data. Change point (CP) analysis was developed to detect distinct changes in time series data. Preliminary reports using CP analysis for fMRI data are promising. Here, we illustrate the application of CP analysis for detecting discrete changes in ambulatory, peripheral physiological data leading up to naturally occurring panic attacks (PAs). The CP method was successful in detecting cardio-respiratory changes that preceded the onset of reported PAs. Furthermore, the changes were unique to the pre-PA period, and were not detected in matched non-PA control periods. The efficacy of our CP method was further validated by detecting patterns of change that were consistent with prominent respiratory theories of panic positing a relation between aberrant respiration and panic etiology.

Longitudinal assessment of physiological data has long been a focus in basic and applied research. Such assessments can offer insight into both chronic and discrete events. Examples for the latter include the examination of recurrent syncopal episodes (Inamdar et al., 2006), ventricular arrhythmias (Krahn et al., 2004), obstructive sleep apnea (Collop, 2008), and/or seizures (Chang et al., 2002). Examples in the area of psychopathology can include the onset of a manic or psychotic episode, or the often dramatic and abrupt occurrence of a panic attack (PA).

The apparent "out-of-the-blue" nature of PAs is intriguing, both from a psychological and biological perspective. Consequently, attempts have been made to capture their physiological profile in laboratory and real-life settings. However studies to date remain sparse and results are mixed. While some studies report physiological arousal immediately prior to and during the reported PAs (Goetz et al., 1993; Taylor et al., 1986; Freedman et al., 1985), others were unable to detect such changes (Gaffney et al., 1988; Hibbert and Pilsbury, 1988). The examination of physiological precursors to naturally occurring PAs poses a unique challenge due to their sudden occurrence. Thus, extended recording times and sophisticated ambulatory monitoring that do not greatly interfere with patients' activities are required. At the same time, as advancements in ambulatory multi-channel technology continue to improve our abilities to record longitudinal data, new challenges of processing and analyzing these data surface. Questions such as the following arise: "When do discrete events occur and how long do they last?", "Are there detectable precursors of psychophysiological events?", and "How do we know that potential events are not simply random noise?" Adding to these challenges is the fact that the obtained biosignals (e.g., heart rate [HR] and respiration rate [RR]) are impacted by confounding variables, such as movement and speech, whose influence must be controlled.

The difficulty in addressing such questions arises, in part, from the apparent lack of appropriate statistical tools to provide meaningful answers to these questions. Most inferential statistics are designed to test specific hypotheses concerning the nature of the data and are not designed to answer questions related to when, and if, changes occur in a time series of data.

1. Current statistical methods for longitudinal physiological data

In the following we describe commonly used statistical methods for the analysis of physiological data. We then illustrate

* Corresponding author. Tel.: +1 214 768 1135; fax: +1 214 768 3910.
** Corresponding author. Tel.: +1 214 768 3422; fax: +1 214 768 3910.
E-mail addresses: drosenfi@smu.edu (D. Rosenfield), ameuret@smu.edu (A.E. Meuret).

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the application of a statistical approach for analyzing longitudinal data that until recently has rarely been used to examine psychophysiological measures.

1.1. Analysis of variance (ANOVA)

Psychophysiologists have typically analyzed longitudinal data from a group (or groups) of individuals using repeated measures ANOVA (Keselman, 1998; Vasey and Thayer, 1987; for a specific example, see Goetz et al., 1993). In the context of longitudinal data, this approach, however, suffers from several disadvantages: First, repeated measures ANOVA requires complete data for each participant. Secondly, traditional repeated measures ANOVA does not allow for time varying covariates. Controlling for movement at each point in the time series could help establish if a change (in cardiac activity, for example) is due to psychological arousal over and above the influence of physical activity. Thirdly, ANOVA is insensitive to discrete, time limited events that occur at some unknown point during a long time series. Finally, repeated measures ANOVA is subject to a number of very restrictive assumptions (e.g., sphericity) which are rarely met (Tabachnick and Fidell, 2007). Although various methods can be used to adjust for violations of these assumptions, such as Greenhouse-Geisser or multivariate approaches to repeated measures ANOVA, the power of these analyses is often reduced by these methods. In sum, ANOVA is not optimally designed to detect a "signal" that might exist in the midst of background noise; consequently the question of relevant change often remains unanswered.

1.2. Mixed models

A more general mixed model approach, such as hierarchical linear modeling (HLM), can effectively deal with some of the limitations of repeated measured ANOVA (Keselman, 1998; Tabachnick and Fidell, 2007). In particular, HLM can easily handle data that are missing at random (Hall et al., 2001; Hamer and Simpson, 2009) and can incorporate time varying covariates (Singer and Willett, 2003). However, mixed models are designed to detect specific, hypothesized, overall trends in the time series beginning at specified time points. They often cannot detect changes of unknown timing and duration, especially if the change is time limited. Different analytical approaches are necessary to answer questions related to discrete, time delimited changes occurring in time series data (Lindquist et al., 2007; Robinson et al., 2010).

2. Change point analysis

Change point (CP) analysis (e.g., Basseville and Nikiforov, 1993; Lindquist et al., 2007) is an approach adapted from statistical control theory that was developed to detect significant changes in time series data. The CP method also allows the examination of various kinds of hypotheses through the imposition of different constraints on the CP parameters. There now exist numerous variations of CP analysis emanating from various fields, such as statistical control theory, econometrics (e.g., Fomby and Lin, 2006), and psychophysiology (Lindquist et al., 2007; Robinson et al., 2010). These various analytic strategies are largely comparable and are designed to detect change points in time series data while at the same time addressing questions unique to their respective fields. Here, we present an application of the CP method to ambulatory, psychophysiological data. Our method is based on statistical control theory, and is designed to be a straightforward, simple application that is aimed at addressing a diverse array of psychophysiological questions. Our application accommodates multiple time series and corrects for the potentially confounding effects of extraneous third variables.

Two applications of CP analysis that could be particularly relevant to psychophysiology are: (1) the detection of the timing and magnitude of a single change point in a time series (single CP analysis), and (2) the detection of the timing, magnitude, and duration of multiple changes in a time series (multiple CP analysis) (see Lindquist et al., 2007). We discuss these applications below.

2.1. Single CP analysis

Single CP analysis is designed to detect a single sustained change in a physiological measure. For example, it can detect a physiological event that might be a trigger of a psychological phenomenon (e.g., an increase in PCO_2 that might lead to hyperventilation and precipitate a PA; or a drop in blood pressure that might result in fainting in patients with blood phobia). Single CP analysis examines each time point in a time series of data to determine if the average level of the outcome variable up to a specific time point (β_0, the mean of the distribution from time 1 to time t_0) is significantly different from the average level of the variable after that time point (β_1, the mean of the distribution from time t_0 to the final time, T). The significance of the difference between β_0 and β_1 is evaluated using the two-sample pooled t-test (Montgomery, 2001, pp. 117–119). The time point at which the CP occurred is calculated using maximum likelihood estimation (MLE) (Basseville and Nikiforov, 1993). The MLE calculates β_0, β_1, and the time t_0 (the MLE estimate of the time of the change point) to maximize the probability that the actual distribution of the data came from distributions with the calculated values for these parameters (that is, distributions with a mean of β_0 that persists through time point t_0, followed by a distribution with mean β_1 which persists to the end of the time series). The formula for the maximum likelihood estimator of the change time can be found in Appendix A of this manuscript.

2.2. Multiple CP analysis

Multiple CP analysis can be used to examine processes that might turn on and off (e.g., evoked potentials) or that might vary substantially over time (e.g., respiratory instability before PAs). While single CP analysis does not allow for the possibility that the data may return to their initial states, or for the possibility that the time series might change more than once, multiple CP analysis allows for these events. In multiple CP analysis, the time series is scanned from the beginning to detect the first CP (the first point at which the distribution changes from one level to another). Then, the remaining time series is scanned for the next change point. This process continues until no more CPs are detected.

3. Study aim

While Lindquist and colleagues (Lindquist et al., 2007; Robinson et al., 2010) have effectively demonstrated how CP analysis can be applied to complex functional magnetic resonance imaging data, the aim of this report was to describe an alternative approach to CP analysis applied to ambulatory, peripheral psychophysiological data, while still drawing from their important work. We analyzed a selection of peripheral parameters that are thought to play a central role in the onset of PAs. Additionally, we present the CP method within the context of accounting for time varying "confounding" variables, such as movement, and providing for comparisons between "experimental" time series (pre-PA) and those from a "control" time period (not preceding a PA). By doing so, we hope to expand the range of application of CP analysis,