

## Topic: Improving the CARWatch Framework for Objective Cortisol Awakening Response Assessment

Experiencing stress is a regular part of our daily life. Although stress can have an increasing effect on our performance [1] prolonged stressful situations can lead to affective disorders like depression [2]. When humans are exposed to stressors the autonomic nervous system (ANS) triggers multiple protective mechanisms such as increasing the heart rate and blood pressure as a response [3]. Additionally, the hypothalamic-pituitary-adrenocortical (HPA) axis is activated, which causes the secretion of glucocorticoids to help distribute additional energy resources depending on the needs [4]. The activation also causes the release of cortisol, a well-established stress marker [3]. An indicator of the basal HPA axis activity is the magnitude of the cortisol awakening response (CAR) [5] which is described as cortisol concentration across the first hour after awakening [6]. Deviations from the CAR pattern are associated with different types of psychosocial factors like job stress or burnout [5]. A typical CAR assessment is performed by taking multiple saliva samples in time intervals of 10 to 15 minutes within the first 30 to 60 minutes after awakening. To make well-founded statements about the CAR, measurements must ideally be taken without any delays as small discrepancies can already lead to incorrect CAR estimates [7]. This requires objective monitoring techniques to reliably determine the time of awakening and the saliva sampling times. Large studies assessing the CAR are mostly conducted in participants' domestic settings to ensure ecological validity which makes it difficult to objectively assess both awakening time and sampling times. According to the 2016 CAR expert consensus guidelines, only few CAR studies (5.6 % between 2013 and 2014) work with objective assessment methods for both times which negatively impacts the measurement validities [8].

To solve this methodological issue, *CARWatch* was developed as an Android app that enables an objective assessment of CAR sampling times. This is done by a built-in alarm that wakes participants and generates additional alarms according to the time intervals in the sampling schedule. The alarms can only be stopped by scanning barcodes attached to the saliva sample tubes [9]. Additionally, researchers can customize various study parameters like the number of samples or sampling intervals via a web interface. Even though *CARWatch* has been proven to reduce delays in sample collection and improve objective measurements of sampling times [9], there are still limitations. The app mostly relies on the user to correctly report the awakening time if they wake up before an alarm, leaving room for error.

The goal of this master's thesis is therefore to enhance and extend the current *CARWatch* framework to make it more accessible and beneficial for the broader research community. This includes extending the existing framework with additional features that improve the usability for both researchers and study participants, such as the development of a web service for real-time tracking of study compliance as well as the integration of smartwatch capabilities to improve the objective assessment of awakening times. Furthermore, feedback from early adopters will be collected to identify limitations and potential enhancements which will then be used to improve the overall *CARWatch* framework. The implementation and subsequent evaluation of these enhancements hopefully help to make *CARWatch* a versatile tool for researchers, potentially contributing to advancements in scientific knowledge within the realm of psychoneuroendocrinological studies.

The proposed work consists of the following parts:

- Literature and patent research of relevant work resulting in a comprehensive list of existing applications and frameworks for objective sampling monitoring of biomarkers in the field
- Implementation of a real-time saliva compliance tracking feature
- Identification of additional areas of improvement for the *CARWatch* framework based on early adopter feedback
- Improving and extending the *CARWatch* framework based on the identified areas of improvement

- Evaluation of CARWatch user behavior from pilot studies, identification of possible determinants of adherence differences (e.g., weekday vs. weekend, morning samples vs. samples throughout the day)
- Optional: Prototyping of an iOS application that fulfills the basic requirements for objective saliva monitoring

The thesis must contain a detailed description of all developed and used algorithms as well as a profound result evaluation and discussion. The implemented code has to be documented and provided. An extended research on literature, existing patents, and related work in the corresponding areas has to be performed.

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## References

- [1] D. M. Diamond, A. M. Campbell, C. R. Park, J. Halonen, and P. R. Zoladz, "The temporal dynamics model of emotional memory processing: A synthesis on the neurobiological basis of stress-induced amnesia, flashbulb and traumatic memories, and the Yerkes-Dodson law", *Neural Plast.*, vol. 2007, 2007, doi: 10.1155/2007/60803
- [2] S. Cohen, D. Janicki-Deverts, and G. E. Miller, "Psychological Stress and Disease", *JAMA*, vol. 298, no. 14, pp. 1685–1687, 2007, doi: 10.1001/jama.298.14.1685
- [3] Y. M. Ulrich-Lai and J. P. Herman, "Neural regulation of endocrine and autonomic stress responses", *Nat. Rev. Neurosci.*, vol. 10, no. 6, pp. 397–409, Jun. 2009, doi: 10.1038/nrn2647
- [4] J. P. Herman, J. M. McKlveen, S. Ghosal, B. Kopp, A. Wulsin, R. Makinson, J. Scheimann, and B. Myers, "Regulation of the Hypothalamic-Pituitary-Adrenocortical Stress Response", *Compr. Physiol.*, vol. 6, no. 2, pp. 603–621, 2016, doi: 10.1002/cphy.c150015
- [5] Y. Chida and A. Steptoe, "Cortisol awakening response and psychosocial factors: A systematic review and meta-analysis", *Biol. Psychol.*, vol. 80, no. 3, pp. 265–278, 2009, doi: 10.1016/j.biopsycho.2008.10.004.
- [6] J.C. Pruessner, O.T. Wolf, D.H. Hellhammer, A. Buske-Kirschbaum, K. Von Auer, S. Jobst, F. Kaspers, C. Kirschbaum, „Free cortisol levels after awakening: a reliable biological marker for the assessment of adrenocortical activity", *Life Sci.*, vol. 61, no. 26, pp. 2539–2549, 1997
- [7] N. Smyth, L. Thorn, F. Hucklebridge, P. Evans, A. Clow, "Post awakening salivary cortisol secretion and trait well-being: the importance of sample timing accuracy", *Psychoneuroendocrinology*, vol. 58, pp. 141–151, 2015, doi: 10.1016/j.psyneuen.2015.04.019.
- [8] T. Stalder, C. Kirschbaum, B. M. Kudielka, E. K. Adam, J. C. Pruessner, S. Wüst, S. Dockray, N. Smyth, P. Evans, D. H. Hellhammer, R. Miller, M. A. Wetherell, S. J. Lupien, A. Clow, "Assessment of the cortisol awakening response: expert consensus guidelines" *Psychoneuroendocrinology*, vol. 63, pp. 414–432, 2016, doi: 10.1016/j.psyneuen.2015.10.010.
- [9] R. Richer, L. Abel, A. Küderle, B. M. Eskofier, and N. Rohleder, "CARWatch – A smartphone application for improving the accuracy of cortisol awakening response sampling", *Psychoneuroendocrinology*, vol. 151, pp. 106073, 2023, doi: 10.1016/j.psyneuen.2023.106073