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INVITED REVIEW

Is salivary alpha-amylase an indicator of autonomic nervous system dysregulations in mental disorders?—A review of preliminary findings and the interactions with cortisol

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Summary During recent years, a growing interest emerged in using salivary alpha-amylase (sAA) as a non-invasive, surrogate marker for sympathetic activity. Numerous studies applying stress protocols have demonstrated that sAA is highly sensitive to stress-related changes (in healthy subjects). Additionally, it was suggested that sAA might moreover serve as an index for pathological dysregulation of the autonomic nervous system (ANS) in patients showing psychopathology. Since then, a small but growing literature investigated sAA in patients with mental disorders. This review aims to give an overview of preliminary findings in this field of research. The results of $n = 15$ studies are described in detail and implications for further research are discussed. Although the number of studies and the samples examined were rather small, changes in sAA, reflecting adrenergic dysregulation, could be demonstrated in psychopathology, especially in anxiety-related disorders.

This field of research is still in its early stages. However, the studies included in this review revealed first evidence that the employment of sAA, as an indicator of ANS dysregulation in mental disorders, is promising.

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1. Introduction

1.1. Characteristics of sAA

Salivary alpha-amylase (sAA) was first described in saliva by Leuchs in the 19th century. It is an enzyme belonging to the family of glycosyl hydrolases and is produced locally in the oral cavity by the salivary glands. Its biological function is the digestion of macromolecules such as carbohydrates and starch (Zakowski and Bruns, 1985). The salivary glands are part of the digestive tract and are comprised of three different types, i.e., the parotid, submandibular and sublingual glands. Salivary alpha-amylase is considered as one of the most important enzymes in saliva and is mainly generated in the parotid glands. ''Whole saliva'' characterizes fluids that derive from different glands, while the secretion of fluid by single glands is referred to as ''duct saliva''. Additionally, there is a distinction between ''resting'' or ''stimulated'' saliva with varying contributions to saliva secretion by the different glands. Under stimulation more than 50% of the total saliva is produced in the parotid glands while it is only 20% in an unstimulated condition (Humphrey and Williamson, 2001). Saliva is mostly produced by acinar cells and its release is under control of neural stimuli. Salivary alpha-amylase is secreted from the salivary glands mainly in response to beta-adrenergic stimuli (Chatterton et al., 1996). Numerous animal studies and the results of human studies have suggested that the autonomic nervous system (ANS) plays an important role in sAA secretion and that beta- but also alpha-adrenergic mechanisms are involved (for more details see: Nater and Rohleder, 2009). Given that the secretion from salivary glands is controlled by direct sympathetic innervation, sAA was proposed to be a surrogate marker of sympathetic nervous system (SNS) activity with changes in sAA reflecting sympathetic influences on salivary glands.

With regard to baseline measures in healthy persons, sAA shows a typical diurnal profile with a sharp decline during the first hour after awakening and a constant increase during the rest of the day with a peak in the late afternoon or evening (Nater et al., 2007; Rohleder et al., 2004).

1.2. Advantages of measurement in saliva

The major advantage of sAA over other parameters reflecting sympathetic nervous system activity (i.e., heart rate measures or skin conductance) is that it is saliva-based. Salivary samples are relatively easy to obtain and can be collected at all times (except during sleep) without being reliant on the assistance of medical staff. Therefore, it is perfectly suited for research in naturalistic environments such as a person's home, working place, i.e., where the participant is going after regular daily activities. A drawback of other autonomic measures obtained by venipuncture such as plasma epinephrine/norepinephrine or other invasive procedures like cerebrospinal fluid (CSF) is that it is (in probands) often accompanied with anxiety or even pain and can potentially serve as a stressor itself which might lead to an acute release of catecholamines and therefore biased data (especially when assessing a standardized stress protocol, i.e., responses to an acute stressor). Thus, eligible subjects could feel discouraged with regard to blood samples, while saliva sampling offers the opportunity to collect data from populations such as anxious or sensitive subjects as well as older subjects, children or even infants. Furthermore, parameters like heart rate and blood pressure — which were regarded to be the gold standard of ANS assessment — are not only easily influenced by these hormones but also by other factors such as posture. Additionally, data suggests that sAA is more sensitive to subtle psychological stress than heart rate or blood pressure (van Stegeren et al., 2006). Moreover, different methods of measurement concerning changes in ANS activity can involve costly apparatus and labour-intensive, complex techniques like for example impedance cardiography or electrocardiograms which are rather inapplicable in field research.

In contrast, given the unproblematic procedure of sampling, it is possible to collect numerous saliva samples in short time intervals illustrating detailed profiles of changes in sAA