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Salivary Biomarkers in Children: Exercise, Physical Activity and Obesity Studies

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ABSTRACT

Worldwide, overweight/obesity and associated chronic diseases such as type 2 diabetes (T2D), have reached epidemic proportions. The current statistics show that overweight/obesity and chronic disease is prevalent amongst adults and children in South Africa. The aim of the review is to discuss current research investigating how overweight/obesity and inactivity impact on salivary biomarkers of immune and sympathetic activation in children and how these may change with weight-loss and increased activity. There is limited research regarding the effect that these factors have on salivary biomarkers of health status, especially in children. Further, research is required to provide a clearer understanding of how salivary biomarkers may be used for understanding the impact of obesity and physical inactivity on paediatric health. This will play a role in the development of appropriate physical activity and exercise guidelines for children.

KEYWORDS: Physical activity; Obesity; Immunity; Neuro-endocrine; Children; Salivary biomarkers; Sympathetic activation.

ABBREVIATIONS: T2D: Type 2 Diabetes; SIgA: Salivary Immunoglobulin A; URTI: Upper Respiratory Tract Infections; Sc: Salivary Cortisol; sT: Salivary Testosterone; PA: Physical Activity; BF: Body Fat; CRF: Cardiorespiratory Fitness; sCRP: Salivary C-reactive protein; sAA: salivary Alpha-Amylase; HR: Heart Rate; IL-6: Interleukin-6; ELISA: Enzyme-linked immunoassay; SNS: Sympathetic Nervous System; RMSSD: Root Mean Square of Successive Differences; HPA: Hypothalamus-Pituitary-Adrenal.

INTRODUCTION

This paper aims to review the current research on salivary biomarkers of immune and sympathetic activation in the fields of physical activity (PA), exercise, obesity and health with a focus on children. The adult population has been the focus of previous research in this area. Overweight/obesity and/or lack of PA have been suggested to have negative effects on immune and neuro-endocrine function.[1,2] Currently, there is limited research worldwide and in South Africa as to the effect these factors have on salivary biomarkers of immune function and sympathetic activation in children. Understanding the relationship between these variables will help in the development of safe and effective PA and exercise prescription guidelines for health and exercise professionals, coaches and teachers. Such guidelines will be particularly relevant for children whose immune function is compromised and/or sympathetic activation is dysfunctional.

SALIVA AS A DIAGNOSTIC TOOL

Saliva contains a certain level of previously circulating elements/molecules that are secreted consistently into the saliva and can be measured using biological assays.[3] Over the past 2 decades, saliva has been advocated as an alternative to blood as a diagnostic fluid. In addition to

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being more straightforward and more economical to obtain than blood, saliva has the added advantage of being easier to handle for diagnostic purposes because it does not clot once it comes in to contact with ambient air.[4] Collection of saliva is non-invasive, painless and convenient and is an important research tool for assessing the health of children.[5] Immune, inflammatory, and neuro-endocrine biomarkers can be measured accurately and reliably in saliva. The following sections will provide an overview of the research examining these biomarkers in children.

IMMUNE BIOMARKER: SALIVARY IMMUNOGLOBULIN-A

Salivary IgA (sIgA) is frequently known as the "first-line of defence" against pathogenic microorganisms, viruses, and bacteria within the immune system and is the dominant immunoglobulin in external secretions that bathe respiratory and intestinal mucosal surfaces.[6] Salivary IgA is undetectable at birth but then consistently increases with age.[7] The levels of sIgA reach their approximate peak by seven years of age and remain consistently high during mid-life and then decline during old age.[7] Gender differences in sIgA levels have been reported in healthy young men and women.[8] Serum levels of IgA have not been shown to have direct relationship with those found in saliva.[7,9-11] In children and the elderly, both who are at increased risk of a compromised immune system, a lower concentration of IgA in saliva has been conceptualized as a risk factor for upper respiratory tract infections (URTI).[9-11] Additional studies have also linked mood, academic stress and social support with altered levels of sIgA.[12,13] Lower levels of sIgA have also been shown to be associated with increased risk for periodontal disease and caries.[14,15]

Salivary IgA is a polypeptide complex comprising 2 IgA monomers, the connecting J chain, and the secretory component.[16] The first mechanism of protection by sIgA occurs at the stromal side of the epithelium.[16] At this location, sIgA can complex with antigens present locally in the underlying tissue. Salivary IgA has been shown to have an early morning acrophase followed by a decline to a stable base some 6 h after awakening.[17]

There is limited research on the effect of moderate intensity training on sIgA, namely in children. sIgA levels were reported to be enhanced in children following moderate intensity exercise, but suppressed following high intensity exercise.[18] This is of significance for coaches working with young athletes who need to ensure that the volume and intensity of exercise sessions do not compromise the immune system leaving the athlete more prone to illness. A study by Tharp[19] on 27 prepubescent boys aged 10-12 years, and 23 post-pubescent boys aged 16-18 years examined sIgA before and after 3 games and 3 practice sessions during the basketball season. Results showed that sIgA levels were significantly elevated following basketball practice and games, suggesting that basketball exercise can increase sIgA levels and that chronic exercise over the basketball season may increase the resting levels of sIgA. These changes may give athletes more protection against respiratory infections both after exercise and in the resting state later in the season.[19] Filaire et al[20] examined the effects of physiological and psychological stress on sIgA in young female gymnasts. A significant reduction in sIgA concentration was found following acute exercise and resting sIgA levels did not seem to be affected by periods of training. They also found no relationship between sIgA and cortisol. A study of adolescent female tennis players (included 17 subjects up to the age of 21) examined the incidence of URTIs and sIgA and found that resting sIgA levels were not affected by periods of training. The study showed that players with the greatest exercise-induced reduction in sIgA secretion rate, but not concentration, had the highest incidence of URTI.[21]

Research has also examined the relationship between PA, obesity and sIgA, URTIs and cortisol. Cieslak et al[22] examined the effect of PA, body fat percentage and salivary cortisol on mucosal immunity in children using a 20 m shuttle run for prediction of aerobic fitness in 29 boys, 32 girls ages 10-11 years. The authors found that sIgA was significantly correlated with reported URTIs and that children who spent more time in sport activities had a higher aerobic fitness and reported fewer "sick" days. Children with a body fat >25% reported more sick days. There was no correlation between sIgA and cortisol.

A study examining the incidence of infections in 10-12 years old children participating in sports found that participation in greater than 5 sports activities per week increased the occurrence of the common cold, cough, fever symptoms, where three to 4 activities per week lowered occurrence.[23] This result suggested a protective mechanism whereby moderate exercise may enhance the immune system, and overexertion may increase susceptibility to illness in children. Jedrychowski et al[24] examined childhood respiratory infections in terms of lifestyle factors and found that overweight children (body mass index (BMI)>20) experienced twice as high a risk of respiratory infections than children with low BMI, independent of PA levels, compared to normal weight children. However, they did not include any information regarding immune function, such as sIgA level. An additional study examined the relationship between PA and URTIs in preadolescent children and found that preadolescent children who had low PA levels had an increased risk of recurrent acute respiratory infections, compared to those that were moderately active and highly active.[25] Pallaroa et al[26] examined the total sIgA, serum C3c and IgA in obese and lean school children between 6-13 years of age and found that obese compared to lean children had a compromised secretory immune system, as indicated by lower levels of total sIgA, without an increased incidence of clinical symptoms and infections.[26] This study further suggested the importance of regular PA for children to not only assist in achieving an optimum weight for their age, but also improve mucosal immunity. In conclusion, the limited research examining the effect of moderate intensity exercise on immune function in normal and overweight children highlights the need to perform further research with this age group.

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INFLAMMATION: SALIVARY C-REACTIVE PROTEIN

It has been suggested that salivary C-reactive protein (CRP) may provide information relating to systemic health status associated with chronic disease.[27] Up to half of all events associated with cardiovascular disease (CVD) are reported to occur in apparently healthy individuals who have few or none of the traditional risk factors, including hyperlipidemia.[28] As a result, there has been increased focus on the role of other factors, such as inflammation, in the development of atherosclerosis and CVD.[28] These efforts have led to the search for inflammatory biomarkers to improve the detection of coronary and cardiovascular risk among seemingly healthy individuals.[29] Prominent among the possible candidates for a clinically useful biomarker of CVD risk is circulating CRP as measured by high-sensitivity (hs) assay. Studies have shown that elevated levels of CRP are associated with inflammation and increased cardiovascular risk.[29] Research has suggested a prognostic association between increased CRP production and outcome after acute myocardial infarction and in acute coronary syndromes.[30]

C-reactive protein, a pentameric protein produced by the liver and is part of the nonspecific acute-phase response during inflammation, infection and tissue damage.[30] C-reactive protein secreted by hepatocytes under the transcriptional control of the cytokine interleukin-6 (IL-6).[30] Salivary CRP is likely to originate from the liver and to mirror serum CRP levels. Therefore, salivary CRP could offer an estimate of systemic inflammation.[31] Recently, a high-sensitivity commercially available enzyme-linked immunoassay (ELISA) adapted to measure CRP in human saliva has become available and may offer a valuable strategy to assess salivary CRP levels in various populations.[31] These authors provided initial evidence suggesting that assessment of CRP in saliva allows for a valid prediction of serum CRP. The researchers found a moderate-to-strong association between CRP measured in saliva and in serum (r=.72, p<.001).[31] The research suggested that salivary CRP may thus facilitate and promote research exploring the correlates of low-grade inflammation in epidemiological studies and make it feasible to expand immune, inflammatory and neuro-endocrine research in children.[31]

CRP has been shown to be strongly related to all anthropometric and direct measures of total and central abdominal obesity, diastolic blood pressure, and apolipoprotein and lipid levels.[32] In one particular study the observation made was that CRP levels were strongly and independently related to directly measured total and central obesity and this is consistent with the finding that adipocytes secrete interleukin-6, the main stimulus for CRP biosynthesis.[30]

There have been numerous studies relating serum CRP and markers of inflammation with physical fitness and obesity measurements in children.[33-37] Although a moderate-to-strong association between CRP measured in saliva and in serum was found,[31] there are only 2 studies relating salivary CRP with measures of physical fitness, obesity or health status in children. The first study[38] examined the relationship between salivary CRP, cardio-respiratory fitness and body composition in 170 black South African children (age 9.41±1.55 years, 100 females, 70 males). Results indicated that poor CRF was independently associated with elevated salivary CRP concentration (OR 3.9, 95% CI 1.7-8.9, p=0.001). Poor CRF (OR 2.7, 95% CI 1.2-6.1, p=0.02) and overweight/obesity (BMI≥85th percentile) (OR 2.5, 95% CI 1.1-5.9, p=0.03) were independent predictors of elevated salivary CRP secretion rate. These results suggest a strong association between poor cardio-respiratory fitness and/or overweight/obesity and inflammatory status in children based on elevated salivary CRP levels. The second study[39] aimed to evaluate the oral inflammatory and humoral immune status in 32 children with allergic asthma and 20 control children. A significant correlation between total protein/haptoglobin and IgG/sIgA for children with allergic asthma was found. The results suggest that the higher salivary levels of CRP and haptoglobin may be markers of allergic inflammation and severity of asthma. Further research is needed to better understand the role salivary CRP, as compared to serum CRP, and markers of inflammation have on physical fitness and obesity measurements in children.

SYMPATHETIC NERVOUS SYSTEM: SALIVARY ALPHA-AMYLASE

The sympathetic nervous system (SNS) is an important regulator of the stress response. Catecholamines, secreted as part of the acute SNS stress response, are difficult to assess in saliva because of the low concentrations and rapid degradation of epinephrine and norepinephrine and the difficulty of stabilizing these hormones in the sample.[40] Other substances co-secreted with catecholamines can serve as an alternative index of adrenergic activity within the SNS and can be reliably measurable in saliva owing to their greater stability.[40]

One of these such alternatives or surrogates for SNS activity is alpha-amylase, which, although not a hormone, shows the same excretion patterns as catecholamines.[40] Therefore if catecholamines are elevated there is a corresponding increase in alpha-amylase in the saliva that indicates increased SNS activity. Because assays for amylase are more easily available in smaller clinical laboratories, saliva analysis of this enzyme may offer an interesting alternative for SNS activity testing.[40] Assessment of salivary alpha-amylase (sAA) as a non-invasive biomarker for the SNS, offers a multitude of possibilities in different research areas and may well become an important parameter in stress research.[41]

Alpha-amylase is one of the major salivary enzymes in humans, and is secreted from the salivary glands in response to SNS stimuli. In acinar cells, release of salivary components is under the control of neuronal stimuli where classic neurotransmitters and specific bioactive peptides serve as the main stimuli for sAA secretion.[41] Determining sAA levels and responses to stressors can provide information about the differences in SNS

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stress response. Normal sAA has a pronounced and distinct diurnal rhythm with a strong drop in activity in the first hour after awakening, and a steady increase towards the evening.[42]

A strong activator of the SNS is PA.[42] Exercise is known to increase sympathetic activity, and the high protein level in saliva following exercise may be due to increased adrenergic activity in the salivary glands.[42] It is suggested that sAA response patterns to both physical and psychological stressors correspond to the response patterns of the SNS.[42] A variety of studies have examined the effects of exercise on sAA, however most of the studies have focused on the adult population.[43-47] These studies suggest that exercise can result in a marked increase in sAA as exercise is known to increase sympathetic activity. High protein level in saliva following exercise is suggested[41] to be due to increased adrenergic activity in the salivary glands.

Capranica et al[48] evaluated the effects of an official taekwondo competition (three 1-min rounds with a 1-min recovery in-between) on heart rate (HR), sAA and salivary-free cortisol (sC) in 12 young (10.4±0.2 years) male taekwondo athletes. Peak sAA was observed at the end of the match (169.6±47.0 U/mL) and was different (p=0.0001) from the other samplings (pre-competition 55.0±14.0 U/mL, 30-min recovery 80.4±17.7 U/mL, 60-min recovery 50.5±7.6 U/ml; 90-min recovery 53.2±9.6 U/mL). These findings confirmed that taekwondo competitions pose a high stress on young athletes.[48] The different sAA and sC reactions in response to the physical stressor mirrored the faster reactivity of the sympathetic-adrenomedullary system relatively to the hypothalamic-pituitary-adrenocortical system.[48] An additional study[47] assessed the effect of an acute bout of high-intensity intermittent laboratory cycling exercise on sIgA concentration and sAA activity in 8 well trained games players and found a five-fold increase in sAA activity (p<0.01 compared with pre-exercise). The increased sAA activity after exercise may improve the protective effect of saliva, since this enzyme is known to inhibit bacterial attachment to oral surfaces.[47] It is difficult to deduce the function of short-term increases in sAA while the biological meaning of transient rises in the anti-bacterial action of the enzyme remains unclear. However, such short-term increases may be useful to the body in that energy is made available by increased digestive action in response to stress.[41] Physiological stress reactions comprise orchestrated actions throughout the body, putting the organism in a state of overall preparedness to engage in fight or flight. Thus, increases in amylase activity may be one of many actions involved in activating the body's resources to cope with stressful events or threats to homeostasis.[41] Further studies are needed to examine long-term changes in sAA concentrations.

There appears to be a possible link between sAA and eating behaviour in children. One study reported a positive association between sAA activity and increased BMI (greater obesity) in adolescent males and females.[49] Another study with men and women (average age 26.7 years (8.8)) found that BMI was negatively associated with average morning sAA. Specifically, there was a 3.4% decrease in average sAA level with each increasing point on the BMI scale.[42] sAA stress reactivity was investigated across different age groups, including 62 children (6-10 years, 32 boys, 30 girls), 78 young adults (20-31 years, 45 men, 33 women), and 74 older adults (59-61 years, 37 men, 37 women).[50] BMI, perceived stress scale, chronic stress screening scale as well as cortisol, heart rate, and root mean square of successive differences (RMSSD) response indices failed to predict stress-induced sAA initially with hierarchical linear regression until the children were included in the analysis. With the inclusion of the children, BMI became an even stronger predictor of stress induced alteration of sAA than age. All analysis revealed that age and BMI were the strongest predictors of sAA increases, whereas subjective stress levels as well as cortisol, HR, and RMSSD response indices failed to predict the sAA stress responses.[50] The research related to sAA, PA and obesity in children is very limited compared to the adult population and indicates that the chronic effect of training and the role of obesity have not been fully examined in pre-pubescent children.

HYPOTHALAMIC PITUITARY ADRENAL AXIS: SALIVARY CORTISOL

Salivary cortisol has emerged as an easy-to-collect, relatively inexpensive, biologic marker of stress.[51] In addition, salivary cortisol levels reflect the biologically active (unbound) fraction of cortisol.[52] Cortisol is lipid-soluble, enabling the molecule to diffuse rapidly from the circulation through the acinar cells of the salivary glands into the saliva, without any influence of salivary flow rate.[53] Although its absolute concentration in the saliva is approximately 30-50% lower than in the blood, its measurement may nonetheless be helpful in evaluating subtle alterations of the HPA in many pathophysiological conditions not classically dependent on relevant endogenous hypercortisolism.[53] Researchers have developed methods for collecting salivary cortisol in children, and recent laboratory techniques have made it possible to detect very small concentrations of cortisol in plasma and saliva.[51] Salivary and serum cortisol in children and adolescents have been shown to correlate strongly (r=0.86 to 0.97).[54,55] Salivary cortisol thus enables the study of hypothalamus-pituitary-adrenal (HPA) axis function in epidemiological cohorts.[56]

The HPA axis is a central component of the body's neuro-endocrine response to stress. Its major end-product, cortisol, has profound effects on mood and behaviour as well as metabolism where exposure to increases in cortisol secretion can result in disruption of HPA axis regulation.[57] The cortisol stress response is kept under control through a negative feedback loop including the pituitary, hypothalamus and hippocampus.[58] Cortisol influences a wide variety of processes, including cardiovascular function, fluid volume and haemorrhage, immunity and inflammation, metabolism, neurobiology, and reproductive physiology.[59] Normal circadian rhythm is comprised of high morning and low afternoon-evening cortisol levels and normal feedback control.[60] However, when the final stage of chronic stress with 'burn-out' of central regulatory systems occurs, the

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result is a net decrease of cortisol output, a flattened diurnal secretory pattern, and inhibition of other endocrine axes, and can result in the Metabolic Syndrome.[60] These observations highlight the importance of the HPA axis (and cortisol regulation) in the control of human health.[60]

Increased levels of cortisol has a significant role to play in the body, and so if the HPA axis is not functioning appropriately this will alter obese individuals (including children's) ability to adapt and function metabolically. Numerous laboratories have reported an association between obesity, particularly central adiposity, and high cortisol concentrations in adults. During exercise, cortisol concentrations have been shown to remain higher in obese than in lean adults demonstrating a greater HPA response to the same exercise intensity with obesity.[61] Although there is a large body of literature devoted to the neuro-endocrine response to exercise in adults, namely that increases in intensity and duration of exercise increase salivary cortisol, the relationship between exercise, PA, overweight/obesity and salivary cortisol in children is not fully understood. One study found that salivary cortisol concentration was decreased by 32% in obese children (8-11 years) from pre- to post-exercise compared to lean children.[61] Another study examined the associations between morning cortisol and adiposity in children (9.6+/-0.9 years) at baseline and a 9-month follow-up.[62] Participants included 649 (301 males, 348 females) children for the cross-sectional analysis and 316 (153 males, 163 females) for the longitudinal analysis. A positive relationship was found between morning salivary cortisol and change in waist circumference over 9-months in overweight children. An additional study[1] investigated whether 12 min of high-intensity exercise performed within a regular school break would lead to an increase in cortisol levels in 53, 4^{th} grade (9-10 years) primary school students. They observed a significant group by test interaction indicating a different pre-to-post-test development for the experimental group compared to the control group. However, the interaction effect was caused by an attenuated cortisol concentration in the control group. The authors argued that the control condition, where the students watched a joyful movie, acted as a distracter, which led to a reduction of general school stress.[1] Another study examining serum and salivary cortisol responses to cycling exercise in male children, 10.6+/-0.2 years found that 30 min of submaximal exercise at 70% of VO_{2max} significantly increased serum cortisol level; and salivary and serum cortisol were correlated during and after exercise.[63] Further research measuring salivary cortisol as a marker of the neuro-endocrine stress response in normal and overweight children and associations with PA will assist in promoting understanding of the roles they play in the paediatric *versus* adult population.

CONCLUSION

Participation in regular moderate intensity PA or exercise appears to enhance mucosal immunity (increase sIgA) in preadolescent children. However, research in this area is limited and currently not conclusive. In contrast, poor fitness and inactivity as well as strenuous training appear to compromise the mucosal immune system thereby increasing the risk of URTIs. Children reporting higher levels of body fat and with greater BMI appear to have lower sIgA levels and a greater incidence of infections.

There is very limited research surrounding salivary CRP and PA, obesity and health status in children. The limited research does, however, suggest a strong association between poor cardiorespiratory fitness (CRF) and/or overweight/obesity and inflammatory status in children based on elevated salivary CRP levels.

Research surrounding sAA indicates that exercise can result in a marked increase in sAA as seen by an increase sympathetic activity *via* increased adrenergic activity in the salivary glands. The limited research suggests exercise may also pose a high stress on young athletes as seen with an increase in sAA. Additionally it appears that BMI may be a strong predictor of stress-induced sAA increases in children.

Greater HPA axis response, as seen by increases in salivary cortisol, appears to be influenced greatly by increases in obesity. Higher salivary cortisol secretions have been observed in obese *versus* lean adults and children alike in response to exercise.

Current research surrounding salivary biomarkers in children highlights the vast gaps that are present with regard to PA and obesity. Table 1 includes a summary of research studies that have focused on the relationships between physical activity, body weight, and salivary biomarkers of immune function, inflammatory status and neuroendocrine activation in children (and in some cases adolescents). The majority of research studies currently focus on the adolescent and adult population. However, parallels cannot always be drawn between pre-pubescent children and those individuals in the post-pubescent population. A limitation in current research is how "children" are defined, as Tanner stages are not always identified and pubescent status is not always readily available. Further research is also needed to examine the role that moderate intensity and chronic exercise and obesity have on salivary biomarkers in children as much of the current research on salivary biomarkers is surrounding higher intensity exercise in the athletic adult population. The current research has suggested that markers of immune function and sympathetic activation can be greatly affected by lack of PA and increases in obesity at a young age, which may continue into adulthood. Understanding the relationship between these variables will help in the development of safe and effective PA and exercise prescription guidelines for health and exercise professionals, coaches and teachers. Such guidelines will be particularly relevant for children whose immune function is compromised and/or sympathetic activation is dysfunctional.

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Author, Year	Participants	Research Focus	Findings
Tharp[19]	27 prepubescent boys (10-12 years) and 23 post-pubescent boys (16-18 years) on basketball teams	Examined saliva levels of sIgA before and after three games and three practice sessions during the basketball season	sIgA levels were slightly but significantly elevated following basketball practice and game situations Indicate that basketball exercise can increase sIgA levels and that chronic exercise over the basketball season may increase the resting levels of sIgA
Filaire et al[20]	12 young female gymnasts (12-15 years)	Physiological and psychological stress and sIgA	Significant reductions in sIgA concentration following acute exercise, resting sIgA levels do not seem to be affected by periods of training ; also found no relationship between sIgA and cortisol
Novas et al[21]	17, young female tennis players (14-21 years)	Incidence of URTIs and sIgA	Resting sIgA levels do not seem to be affected by periods of training Those with greatest exercise-induced reduction in sIgA secretion rate, but not concentration, also had the highest incidence of upper respiratory tract infection.
Dorrington et al[18]	15 boys and 14 girls (8-12 years)	Effect of exercise intensity on sIgA in children	sIgA levels were reported to be enhanced following moderate intensity exercise, but depressed following high intensity
Thomas et al[64]	17 old boys (15-16 years)	Effect of repeated bouts of short-term, high-intensity cycling exercise on the sC, sT and sIgA concentrations All participants completed 6×8 s sprints, interspersed with 30 s recovery intervals on a cycle ergometer	The increases in sT and sC reported in this study confirm that repeated bouts of short-term, high-intensity exercise produces significant physiological hormonal responses in adolescent boys, but does not affect mucosal immune function.
Cieslak et al[22]	29 boys, 32 girls (10-11 years)	Effects if of PA, BF, and sC on mucosal immunity in children using 20 m shuttle run for prediction of aerobic fitness	SIgA sig correlated with reported URTIs. Children who spent more time in sport activities and had higher aerobic fitness reported fewer "sick" days. Children with BF >25% more sick days; also no correlation between sIgA and sC.
Pallaroa et al[27]	Obese and lean children (6-13 years)	Examined the total sIgA, serum C3c and IgA levels	Obese children showed lower levels of sIgA than lean children
Thomas et al[65]	19 girls (15-16 years)	Completed 668 s sprints, interspersed with 30 s recovery intervals on a cycle ergometer.	Showed no changes in salivary testosterone, cortisol or IgA following repeated bouts of supramaximal cycling (p>0.05)
Naidoo et al[38]	170 black South African children, 100 females, 70 males (7-12 years)	Relationship between sCRP, CRF, and body composition	Strong association between poor CRF and/or overweight/obesity and inflammatory status with elevated sCRP
Capranica et al[48]	12 male taekwondo athletes (10-11 years)	Examined taekwondo competition on HR, sAA and sC	Peak sAA at end of match was different compared to pre and 30,60, 90 min. recovery values

Table 1: Research studies examining the relationships between physical activity, body weight, and salivary biomarkers of immune function, inflammatory status and neuroendocrine activation in children.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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