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A comparison of changes in secretory immunoglobulin A following a stress-inducing and stress-reducing task

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Summary
Research suggests that the immune system may be adversely affected by chronic stress. There is some evidence that relaxation-based practices may effect an increase in immune functioning, but recent findings suggest that acute stress may lead to similar increases. Given this, we used a counterbalanced within-subjects design to directly compare the effects of a stressful mental arithmetic task and a relaxation-based task on secretory immunoglobulin A (S-IgA). Thirty participants were seen in small groups of two or three where they were administered both a mental arithmetic (stress) task and a relaxing hypnosis task. Four-minute timed saliva samples were obtained immediately following the two experimental tasks and following two baseline periods. Results demonstrated that, compared with baseline, S-IgA concentration and secretion rate were significantly higher following both the relaxation-based task and stress task. Additionally, our data showed that the increases were short-lived, decreasing significantly within 8 min following the completion of each task. Our results indicate that both stress-reducing and stress-inducing tasks can increase S-IgA levels, and these results are discussed with reference to the potential differential mechanisms and clinical significance of such changes. Copyright © 2008 John Wiley & Sons, Ltd.

Key Words
hypnosis; relaxation; immune; stress; S-IgA; psychoneuroimmunology

Introduction

Secretory immunoglobulin A (S-IgA) is one of five classes of immunoglobulins found in serum and secretory fluids, including saliva, breast milk, and nasal, gastrointestinal and bronchial secretions. S-IgA is the major class of immunoglobulins in mucosal secretions and is considered to be a major effector of host defence against microorganisms causing illnesses such as upper respiratory tract infections (Tomasi & Plaut, 1985). The presence of S-IgA antibodies in the fluids bathing mucosal surfaces provides an important first line of defence against infection (Tomasi & Grey, 1972), and the concentrations of S-IgA in mucosal fluids such as saliva have been found to correlate

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more closely with resistance to certain viruses than do serum antibodies or other immune parameters (Liew, Russell, Appleyard, Brand, & Beale, 1984; Murphy et al., 1982).

S-IgA levels may be reduced in the presence of chronic stress (see Valdimarsdottir & Stone, 1997, for a review) and under high workload situations (Wetherell & Sidgreaves, 2005). An inverse relationship between psychological stress and S-IgA levels has repeatedly been demonstrated (Mocci & Bullitta, 2006; Ng et al., 1999; Ng et al., 2004; Phillips et al., 2006; Yang et al., 2002), and when examined alongside cortisol levels, basal S-IgA levels may be a predictor of health outcomes during stressful periods (Volkmann & Weekes, 2006). The evidence that stress can affect the immune system, including S-IgA, raises the possibility that positive experiences, the opposite of stressful ones, could also affect the activity of the immune system. The potential for psychological techniques to *increase* S-IgA levels has been demonstrated by a number of researchers. There is increasing evidence that mental imagery (Jasnoski & Kugler, 1987; Rider et al., 1990), relaxation (Green & Green, 1987; Hewson-Bower & Drummond, 1996; Taniguchi, Hirokawa, Tsuchiya, & Kawakami, 2007), watching humorous videotapes (Dillon, Minchoff, & Baker, 1985; McClelland & Cheriff, 1997), poetry writing (Lowe, Beckett, & Lowe, 2003), progressive muscle relaxation (Lowe, Bland, Greenman, Kirkpatrick, & Lowe, 2001; Pawlow & Jones, 2005) and hypnosis (Olness, Culbert, & Uden, 1989) are effective procedures for increasing salivary S-IgA levels. In the hypnosis study (Olness et al., 1989), specific suggestions to increase immune substances in the saliva were given to children during hypnosis and were found to increase S-IgA concentrations.

Such results have seemed an encouraging first step for developing strategies to boost the immune system. In general, the observed increases are seen in a positive light, reasoning that as stress generally leads to a down-regulation of immune functioning, then interventions that increase immune components must be favourable. However, the concept that stress necessarily leads to decreases in immune components has been challenged by a number of studies conducted during the last decade. Although it is still widely agreed that chronic stress decreases immune functioning, there is growing evidence that acute stress can actually lead to an increase in several measures of immunity in both laboratory (Benham, 2007; Carroll et al., 1996; Ring et al., 1999; Ring et al., 2000; Willemsen, Ring, McKeever, & Carroll, 2000; Winzer et al., 1999) and naturalistic (Evans et al., 1994) settings.

Thus, not only is there disagreement about the clinical relevance of psychosocially induced immunomodulation, but also the relationship between experienced stress/relaxation and increased levels of immunoglobulins appears to be more complex than originally suspected. Direct comparisons of the various stress-inducing and stress-reducing studies are rendered impracticable because of large inter-individual variability in S-IgA levels and the differing methods used to sample and assess S-IgA. To our knowledge, the current study is the first to incorporate both stress-inducing and stress-reducing techniques in a within-subjects design, using two interventions that have previously been shown to be associated with increased levels of S-IgA. We directly compare the extent and duration of stress-induced S-IgA changes to the extent and duration of relaxation-induced S-IgA changes. In so doing, we: (1) test whether each of these interventions do in fact lead to increased S-IgA in our laboratory, and (2) gain some understanding of their relative effectiveness in this regard.

Methods

Participants

Thirty undergraduate students (14 males, 16 females) at the University of Tennessee, Knoxville, participated in this study. Participants were recruited from a pool of students who had recently been assessed for hypnotic susceptibility using a group-administered scale, the Waterloo-Stanford Group Scale (WSGS) of hypnotic susceptibility (Bowers, 1998). Selection of participants was not dependent on the obtained hypnotic susceptibility scores. All participants were 18 years or older [(M = 22.93, standard deviation (SD) = 6.97]. Five of the participants were cigarette smokers.

Mental arithmetic and hypnosis tasks

The Paced Auditory Serial Addition Task (PASAT). The PASAT is an 8-min task designed to act as an acute mental stressor. During the task, participants are required to add two

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sequentially presented single-digit numbers from 1 to 9 while retaining the latter of the two numbers in memory for subsequent addition to the next number presented. Numbers are delivered via an audio tape player, and participants are instructed to write down their answers on a tabulated sheet of paper. The task consists of four 2-min series of 50, 60, 75 and 100 digits at presentation rates of 2.4, 2.0, 1.6 and 1.2, respectively. The tape used was a direct copy of the recording used in previous research (Ring et al., 1999) (with permission).

Hypnosis task. The hypnosis task was modelled on a procedure previously shown to be effective in increasing S-IgA (Olness et al., 1989). The task lasted 16 min and was administered via a pre-recorded audio tape in order to maintain consistency of task administration. The task began with a standardized hypnotic induction that incorporated suggestions of relaxation and focused breathing. The induction was followed by specific suggestions for increasing immune components in the saliva, involving imagery of S-IgA being released into the mouth.

Quantitative measures

S-IgA measures. During the study, four timed samples of saliva were obtained from each participant in order to determine S-IgA concentration and secretion rate following each condition. The volume of the saliva samples from each subject was calculated from sample weight in order to determine saliva flow rates (volume per time: mL/min). Saliva samples were centrifuged for 10 min. Supernatants were aliquotted and stored in microcentrifuge tubes at –20°C for analyses. Saliva samples were analysed for total S-IgA concentration using the sandwich enzyme-linked immunosorbent assay. This procedure was conducted using a commercially available kit (Alpco Diagnostics, Windham, NH, USA). Supernatant from samples were diluted 1 : 2000 in wash buffer. A 96-well pre-coated microtitre plate was then washed five times with 250 µL of wash buffer. One hundred microlitres of five standards (known S-IgA concentrations) and samples were micropipetted into the wells of the microtitre plate. All samples were analysed in duplicate. The plate was then incubated for 1 h on a plate shaker at room temperature, and each well was then aspirated and washed five times with 250 µL of wash buffer. 100 µL of pre-diluted, peroxidase-labelled antibody was then added to each well, and the plate was again incubated for 1 h on a plate shaker at room temperature. After incubation, each well was aspirated and washed five times with 250 µL wash buffer. One hundred microlitres of TMB substrate solution was then added to each well, and the plate was incubated for 5–15 min at room temperature until the colour differences were obvious. Fifty microlitres of stop solution was then added to each well. The colour intensity was measured by a spectrophotometer using a wavelength of 405 nm. The average of absorbance values was used as the representative value. The concentration of IgA (µg/mL) was determined by the standard curve formula (regression formula) for each plate. Salivary IgA concentrations were multiplied by saliva flow rates to determine salivary IgA secretion rates (µg/min).

Heart rate measures. Each participant was fitted with a heart rate monitor (Polar Accurex Plus™, Polar Electro Inc., Woodbury, NY, USA) at the beginning of the experimental session. Heart rate was automatically recorded at 5 s intervals for subsequent analysis.

Post-experiment questionnaire. In order to examine the participants' subjective experiences during the procedure, a questionnaire was administered at the end of the experiment. The questionnaire prompted for some basic demographic information and included a Likert-type scale that assessed the experience of relaxation/stress (–5 = extremely relaxing through 0 = no change to +5 = extremely stressful) during both the stress and hypnosis task.

Hypnotic susceptibility measure. In order to investigate whether any relationship between hypnotic susceptibility and changes in S-IgA existed, participants were administered a group scale of hypnotic susceptibility, the WSGS of hypnotic susceptibility (Bowers, 1998), approximately 2 weeks prior to the experimental session. The WSGS involves a hypnotic induction incorporating suggestions of relaxation, followed by 12 suggestions for the participant to experience various events. The present study used a modified version of the WSGS in which an age regression suggestion was not administered. Thus, the possible range of hypnotic susceptibility scores in this study was from 0 to 11.

Procedure

Participants were instructed to refrain from smoking and any consumption of food 1 h prior to their scheduled session, and to only drink water. Participants were seen in groups of two or three during the mid-afternoon. In accordance with previous research (Ring et al., 1999), the experimenter announced that once all participants have completed the study, the person with the best score on the mental arithmetic task will receive a US$25 gift certificate. Heart rate monitoring was then started and continued until the end of the session.

Participants were instructed to sit quietly while they watched a video on immune functioning (video produced by the experimenter, 3 min in length) that described the basic function and production of S-IgA. Following the video, participants were asked to sit quietly for an 8-min rest period. During this 8-min period, participants watched a video of fish around a coral reef ('Coral Sea Dreaming', Small World Music, Inc., DVD International, West Caldwell, NJ). The use of this video has been suggested as a preferred methodology for the collection of baseline physiological data in that it controls for the effects of anticipation, recollection of the day's events or anxiety that may affect participants' resting levels (Piferi, Kline, Younger, & Lawler, 2000). Immediately following the 8-min rest period, the experimenter instructed participants to wash out their mouths with distilled water and collect their saliva for a 4-min timed interval in a 50 mL graduated tube, which were then stored in an ice chest until completion of the session. Participants were then administered the mental arithmetic task and hypnosis task in a counterbalanced order. Figure 1 shows a flow chart of the PASAT and hypnosis task administration.

In between the two tasks, in keeping with previous research (Willemsen, Ring, McKeever, & Carroll, 2000), a second 8-min rest period was conducted, with participants once again instructed to sit quietly while they watched the coral reef video. To ascertain whether S-IgA levels remained significantly elevated post-hypnosis or PASAT, a second baseline measure of S-IgA was taken at the end of this second rest period. Following each task (PASAT and hypnosis), participants were again asked to produce a timed saliva sample. In total, four saliva samples (two rest/baseline samples, a post-hypnosis sample and a post-PASAT sample) were collected from each participant. Following collection of the final saliva sample, participants completed the post-experiment questionnaire and were fully debriefed.

Data reduction and analysis. S-IgA concentrations and secretion rates were obtained from the samples taken immediately after the initial baseline, the first task, the second baseline and the second task. A repeated-measures multivariate analysis of variance (MANOVA) was applied separately to each task to examine the impact of each task on secretory activity. A repeated-measures MANOVA was also used to compare S-IgA differences between the two tasks (PASAT and hypnosis). Data that exceeded 2.5 SD from the mean were considered outliers and were excluded from analysis.

Heart rate was averaged for each baseline period and each task period, resulting in four

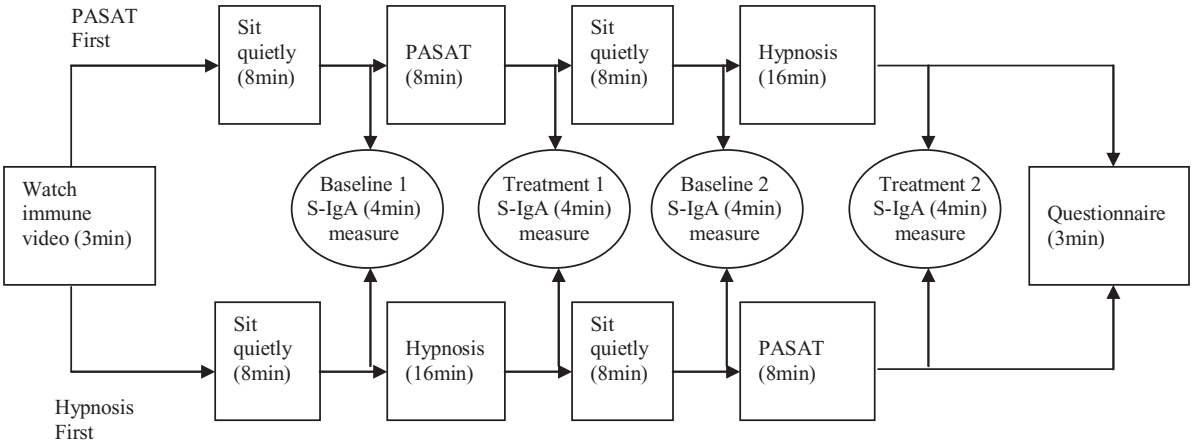

Figure 1. Flowchart of counterbalanced Paced Auditory Serial Addition Task and hypnosis task administration.

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mean heart rate values for each participant. A repeated-measures analysis of variance (ANOVA) was used to compare participants' mean heart rates during the PASAT and hypnosis conditions. Two separate repeated-measures ANOVAs were also applied to each task (PASAT and hypnosis) separately to examine changes from their respective baselines.

Results

Table I shows means and SDs for pre-task (baseline) and post-task S-IgA measures and heart rate. The first baseline measure was significantly higher than the second baseline measure. Some researchers argue against the use of the initial baseline measure in analyses of psychophysiological data (Dobkin, Letourneau, & Breault, 1994). Given that the first baseline measure may have been artificially elevated because of task novelty, we elected to compare post-PASAT and post-hypnosis S-IgA levels to the second baseline levels regardless of order of task presentation.

Manipulation check

In order to establish whether the PASAT and hypnosis task succeeded in being stressful and relaxing, respectively, we examined physiological (heart rate) and subjective (questionnaire) measures. Repeated-measures ANOVAs indicated that the PASAT resulted in a significant increase in heart rate above baseline [$F(1.29) = 44.68$, $p < 0.001$ ($\eta^2 = 0.61$, power = 1.00)], and hypnosis resulted in a significant decrease [$F(1.29) = 7.22$, $p < 0.05$ ($\eta^2 = 0.199$, power = 0.74)].

Self-reports from the post-session questionnaire established that the PASAT was experienced as stressful [M = +2.9, SD = 1.30, $t(29) = 12.26$, $p < 0.001$], and the hypnosis task relaxing [M = −3.5, SD = 1.11, $t(29) = 17.33$, $p < 0.001$].

Salivary measures

Figure 2 shows a rise in S-IgA concentration and secretion rate following both the PASAT and hypnosis task. For the PASAT, a repeated-measures MANOVA revealed that this increase was significant [$F(2.26) = 6.71$, $p < 0.005$ ($\eta^2 = 0.34$, power = 0.88)], and subsequent univariate repeated-measures ANOVAs applied separately to concentration and secretion rate revealed that both of these measures of S-IgA increased significantly [concentration, $F(1.27) = 13.93$, $p < 0.005$, $\eta^2 = 0.34$, power = 0.95; secretion rate, $F(1.27) = 11.22$, $p < 0.005$, $\eta^2 = 0.29$, power = 0.90].

A repeated-measures MANOVA revealed that the hypnosis task also resulted in a significant increase in S-IgA above baseline [$F(2.27) = 18.81$, $p < 0.001$ ($\eta^2 = 0.582$, power = 1.00]. Subsequent univariate repeated-measures ANOVAs demonstrated that this effect was significant for both concentration and secretion rate [concentration, $F(1.28) = 38.90$, $p < 0.001$, $\eta^2 = 0.581$, power = 1.00; secretion rate, $F(1.28) = 23.79$, $p < 0.001$, $\eta^2 = 0.46$, power = 1.00].

A repeated-measures MANOVA was used to examine whether any significant difference existed between the post-PASAT and post-Hypnosis S-IgA measures. There was a significant main effect for task type, with S-IgA significantly higher post-hypnosis than post-PASAT [$F(2.27) = 4.83$, $p < 0.05$ ($\eta^2 = 0.26$, power = 0.75)]. Subsequent

Table I. Means (M) and standard deviations (SD) of S-IgA and heart rate measures.

	S-IgA concentration (μg/mL)		S-IgA secretion rate (μg/min)		Heart rate (bpm)	
	M	(SD)	M	(SD)	M	(SD)
Baseline 1	301.61	(111.62)	150.26	(81.34)	76.00	(12.32)
PASAT	243.35	(153.96)	134.59	(68.94)	82.07	(12.51)
Baseline 2	147.52	(127.29)	87.50	(74.91)	73.20	(11.71)
Hypnosis	313.17	(161.97)	175.36	(97.47)	71.97	(11.70)

Note: Stress and hypnosis manipulations presented in counterbalanced order.
S-IgA: secretory immunoglobulin A; bpm: beats per minute; PASAT: Paced Auditory Serial Addition Task.

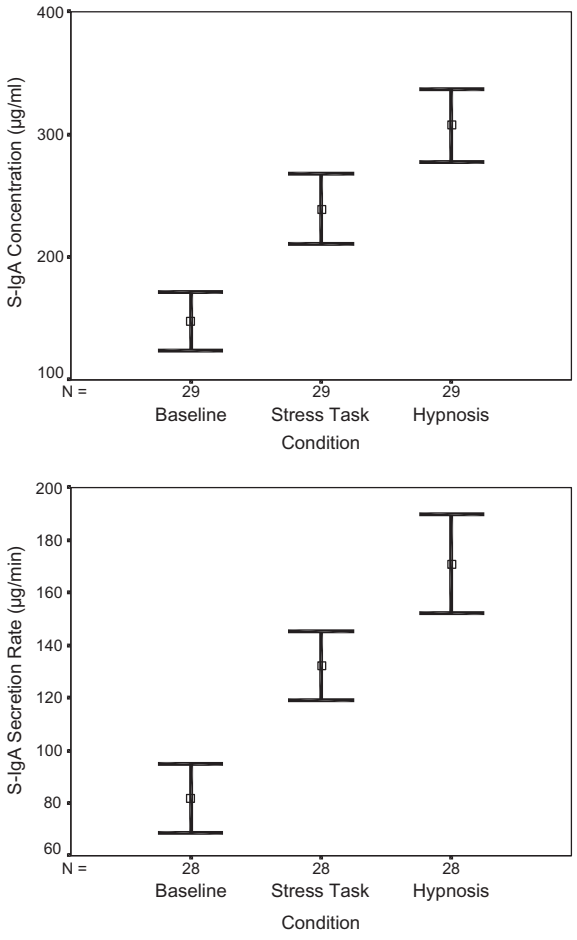

Figure 2. Mean S-IgA concentration (µg/mL) and secretion rate (µg/min) from samples collected immediately following the second baseline, the PASAT, and the hypnosis task. S-IgA: secretory immunoglobulin A; PASAT: Paced Auditory Serial Addition Task.

univariate repeated-measures ANOVAs revealed that differences in S-IgA were significant for concentration [$F(1.28) = 9.87$, $p < 0.005$ ($\eta^2 = 0.26$, power = 0.86)], and for secretion rate [$F(1.28) = 5.52$, $p < 0.05$ ($\eta^2 = 0.17$, power = 0.62)]. Saliva flow rate was not significantly different between the PASAT and hypnosis task [$F(1.29) = 4.07$, $p > 0.05$].

Supplemental analyses

The relationship of hypnotic susceptibility to changes in S-IgA. A bivariate correlation between scores on the WSGS and change in S-IgA following the hypnosis task was not significant for concentration [$r(30) = 0.07$, $p > 0.05$] or secretion rate [$r(30) = 0.20$, $p > 0.05$], indicating that hypnotizability had no relationship to the observed changes following the hypnosis procedure.

Relationship between subjective ratings and changes in S-IgA. A bivariate correlation between subjective ratings of stress or relaxation and changes in S-IgA was not significant for the stress task [concentration, $r(29) = -0.07$, $p > 0.05$; secretion rate, $r(28) = -0.11$, $p > 0.05$] or the hypnosis task [concentration, $r(29) = 0.14$, $p > 0.05$; secretion rate, $r(29) = 0.22$, $p > 0.05$], indicating that subjective stress or relaxation measures had no relationship to observed increases.

Discussion

The results support the notion that both a relaxing and a stressful task, established by both physiological and subjective measures, can cause acute increases in S-IgA. Such results suggest that increases in S-IgA can potentially be driven by different physiological mechanisms. Unlike many previous studies examining increases resulting from either a stressful or a relaxing task, the present study incorporated both manipulations in order to compare their relative effectiveness. A comparison of post-stress task and post-hypnosis task S-IgA measures showed that the relaxation-based hypnosis task resulted in significantly higher levels of S-IgA (both concentration and secretion rate) than the stress task.

A number of previous acute stress studies have employed a second baseline measure following the stress task, demonstrating short-lived effects of acute stress on S-IgA. However, prior research in relaxation-based techniques has invariably involved a design consisting of a single pre-treatment baseline measure and a single post-treatment measure. Although researchers have shown significant effects for hypnosis (Olness et al., 1989), relaxation (Green & Green, 1987), imagery (Rider et al., 1990), music (McCraty, Atkinson, Rein, & Watkins, 1996) and humour (McClelland & Cheriff, 1997), none of the aforementioned studies included a follow-up measure after the initial post-treatment measure. The researchers were thus unable to examine the longevity of the reported immune increases following treatment. In a recent study (Reid, Mackinnon,

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& Drummond, 2001), the authors again found a significant increase in S-IgA immediately after a relaxation procedure but showed that it had returned to baseline levels when measured again some days later. The authors suggested that transient increases after regular episodes of relaxation might help to protect against upper respiratory tract infection. The present study incorporated a second baseline measurement to verify whether S-IgA levels had returned to pre-task levels prior to the second task. For the participants who were administered the hypnosis task first, this second baseline acted as a measure of the extent to which S-IgA increases endured. The results demonstrated that although the hypnosis task was a powerful technique for increasing S-IgA, the effects were short-lived. Within an 8-min resting condition immediately following the hypnosis task, S-IgA levels had returned to the pre-task baseline level. These rapid changes are in keeping with recent research examining the pattern of S-IgA changes both during and following an acute stress task (Benham, 2007), which demonstrated a decrease in S-IgA to baseline levels within 6 min of stress-task completion.

Our results are based on an analysis using the second (lowest) baseline. The issue of baseline is an important one, yet psychophysiological researchers have yet to reach consensus on what is considered a valid and reliable assessment of baseline. Pollak (1991) has emphasized the importance of the baseline period in cardiovascular reactivity studies and argued that inconsistencies in baseline procedures could be a potential reason for inconsistent results. Similarly, Obrist, Light, James, and Strogatz (1987) stated that the conditions under which baseline measurements are recorded might determine whether an expected relationship emerges. One recommendation, which we followed in our design, is that researchers should employ a minimally demanding task to decrease the variability of participants' experience during baseline (Piferi et al., 2000). The purpose of this task (watching an aquatic video) is to allow participants to more readily reach a relaxed state during baseline assessment, and research has demonstrated that it is more effective in achieving this than sitting quietly (Piferi et al., 2000). Despite the use of this baseline task, our second baseline measure was significantly lower than the first baseline measure for heart rate, S-IgA concentration and S-IgA secretion rate. It is possible that the first baseline reflects a normal resting baseline and that the second baseline measure is artificially lowered because of a 'rebound effect' following the termination of the PASAT and hypnosis task. However, it is also possible that the first baseline was artificially elevated because of initial anxiety regarding the experimental setting or anticipation towards the upcoming tasks.

Based on research investigating baseline measures, Dobkin et al. (1994) concluded that it is preferable *not* to use initial baseline measures in analyses of psychophysiological data. For this reason, we chose to examine the data in relation to the second baseline. Our results would have been slightly different had we favoured the pre-task baselines: the hypnosis task still demonstrated significant increases, whereas the PASAT task failed to reach statistical significance. Thus, although the pattern of results remains consistent, in our study, the significance of S-IgA changes following the PASAT was dependent on which baseline measure was used as a comparison.

Lastly, one possible confound in this study was the difference between the duration of the hypnosis task (16 min) and the PASAT (8 min). It could be argued that the hypnosis task produced higher levels of S-IgA than the PASAT simply because the manipulation lasted longer. Recent research (Ring, Drayson, Walkey, Dale, & Carroll, 2002) has examined the effects of prolonged PASAT administration, comparing S-IgA levels after 16 min and after 32 min of the stress task. Significant increases in S-IgA at 16 min were sustained throughout the extended task but showed no consistent increase or decrease as the task was prolonged. Although this does not discount the possible confound of task duration, it suggests that there may not be a conclusive bias.

Mechanisms underlying the observed increases in S-IgA

Although stress-induced activation of the hypothalamic pituitary adrenal axis influences immune function (Webster, Elenkov, & Chrousos, 1997), there is a time lag before cortisol increases (Kirschbaum, Pirke, & Hellhammer, 1993) and a further delay before these cortisol-dependent immunological changes are observed (Munck & Guyre, 1991). Therefore, the rapid changes observed for S-IgA in response to the PASAT have to be mediated through another mechanism. One suggested candidate is the rapidly acting sympathetic nervous system. The sympathetic nervous system

modulates immune function (Felten et al., 1998): noradrenergic sympathetic nerves innervate lymphoid organs, adrenoreceptors are present on lymphocytes and adrenergic agonists influence antibody production. Additionally, Carpenter, Garrett, Hartley and Proctor (1998) reported that sympathetic stimulation of submandibular glands in rats resulted in a sixfold increase in S-IgA secretion. However, Winzer et al. (1999) demonstrated that administration of a selective adrenergic blockade (propranolol) to participants had no effect in dampening the increase in S-IgA concentration following the PASAT. The authors concluded that although stress-related increases in certain cellular components can be blocked with propranolol (Benschop et al., 1994), increases in S-IgA concentration during mental stress were not beta-adrenergically mediated.

Carpenter et al. (1998) found that although the submandibular gland of rats is enervated by both sympathetic and parasympathetic nerves, stimulation of the sympathetic nerves resulted in an S-IgA secretion rate approximately two times greater than the S-IgA secretion rate achieved by parasympathetic nerve stimulation. However, the fact that both sympathetic and parasympathetic pathways exist to the S-IgA secreting submandibular glands may explain how two tasks that differ so much in terms of the associated autonomic responses (indexed by heart rate) can both result in an increase in S-IgA. Based on this animal model, it is possible that the PASAT causes sympathetic activation of the submandibular glands, whereas the hypnosis task results in parasympathetic activation. One other finding from the animal research is suggestive. In anaesthetized rats, S-IgA was found to accumulate in the submandibular gland if it were unstimulated. It was suggested that when the gland was stimulated after a period of non-stimulation, it expelled the accumulated material (S-IgA). Results showed that as the length of the rest period was extended, a nearly linear increase in the amount of S-IgA secreted into the saliva occurred, suggesting a steady accumulation of S-IgA occurs within the gland with time. This may be a possible confound for the hypnosis task. If the task results in the simple accumulation of S-IgA over time (16-min task) because the glands are relatively unstimulated during hypnosis, then the stimulation that occurs following the hypnotic de-induction may be the only event causing the apparent increase in S-IgA levels post-hypnosis. Direct assessment of this mechanism, involving the collection of S-IgA at various intervals during hypnosis, would aid in evaluating this potential confound.

A study by Clow, Lambert, Evans, Hucklebridge and Higuchi (2003) examined the influence of lateralized temporo-parietal-occipital cortex transcranial magnetic stimulation (TMS) on S-IgA. TMS works by generating a magnetic field that penetrates the skull and induces an electric current in the underlying cerebral cortex. A significant increase in S-IgA was shown following left-sided stimulation that, unlike a corresponding increase with right-sided stimulation, was not associated with sympathetic activation. Such studies might shed light on the possible dual mechanisms of S-IgA production, again generating testable hypotheses for why two such dissimilar experiences can produce similar immune responses (increase in S-IgA).

Finally, it is possible that the increase in S-IgA may simply be a result of absorption in a task; that whether a task is relaxing or stressful is less important than whether the task absorbs the person's attention. While this is an intriguing idea, one early study suggests that focused attention is not sufficient to increase S-IgA. Jasnoski and Kugler (1987) found increases in S-IgA for both a relaxation task and a relaxation with imagery task, but not for a vigilance task in which subjects discriminated between tones. However, further research would be needed to assess whether the notion of absorption can be ruled out entirely.

Clinical significance

The current research is in agreement with other investigations that employed relaxation-based manipulations to produce statistically significant elevations of S-IgA. Having established this effect, one must subsequently address the clinical significance of such findings. The importance of S-IgA as a first line of defence against upper respiratory illness, caries and oral infections has been suggested by a number of researchers (Gregory, Kim, Kindle, Hobbs, & Lloyd, 1992; Hanson, Björkander, & Oxelius, 1983; Jemmott & McClelland, 1989; Muller et al., 1992). However, given that a cause and effect between low levels of S-IgA and illness has not been demonstrated, S-IgA levels are best viewed as a risk factor for developing infection.

Assuming that a causal link between lowered S-IgA and illness can be substantiated, the second issue in establishing clinical significance is whether

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the acute increases in S-IgA following relaxation-based techniques can be prolonged. The current study indicates that the effects of the relaxation task are short-lived. Increases in immune components following brief psychological techniques such as relaxation, hypnosis, imagery, etc., are frequently viewed as positive ('immunoenhancement'), but there is insufficient research to conclusively suggest that such techniques can be used to improve immune functioning in the long term or even that successfully increasing immune components will necessarily confer added protection against infection. While techniques to increase S-IgA are unlikely to offer much help for conditions such as selective S-IgA deficiency, it is tempting to speculate that individuals with recurrent upper respiratory tract infections who have a tendency for low S-IgA may find some clinical benefit. Hewson-Bower and Drummond (1996) found that relaxation-based increases in S-IgA could be achieved by both 'healthy' children and those with recurrent upper respiratory tract infection. The same researchers subsequently demonstrated that an extended programme of relaxation-based treatment sessions significantly raised S-IgA levels over the course of treatment and, perhaps most importantly, also reduced cold and flu symptom duration (Hewson-Bower & Drummond, 2001). While far from conclusive, such studies suggest that the findings from ongoing basic research may lead to the development of clinically significant approaches.

Conclusions

Research indicates that stress-reducing techniques can significantly increase the levels of S-IgA in the saliva. The current research suggests that this effect is as potent as increases resulting from a stress-inducing task and also demonstrates that the two types of procedure can be distinguished by both experiential (questionnaire) and physiological (heart rate) measures. However, based on the current investigation, the increases following hypnotic treatment are short-lived. Future research will need to establish the long-term effects of relaxation-based techniques in providing enhanced immunological protection from infection.

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