Longitudinal Analysis of Parotid and Submandibular Salivary Flow Rates in Healthy, Different-Aged Adults

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Background. Early studies suggested that salivary gland dysfunction was a normal sequela of aging. Recent research on healthy, different-aged adults has led to a revision of these former conclusions. Parotid gland function appears to be age-stable, yet there is no consensus on submandibular/sublingual output. To date, there have only been two longitudinal studies utilizing healthy individuals examining parotid function, and no published longitudinal studies on submandibular/sublingual output. The purpose of this study was to examine unstimulated and stimulated major salivary gland flow rates in unmedicated, essentially healthy subjects, over a 3-year period.

Methods. Thirty-seven males and females, aged 26–90 years of age, were examined twice over a 3-year period at the Clinical Center of the National Institutes of Health. All were healthy, community-dwelling adults, without any systemic diseases, and not taking any medications. Unstimulated and 2% citrate-stimulated parotid and submandibular/sublingual salivary gland flow rates were assessed at both visits, and changes over time were evaluated according to the subject’s age at initial visit.

Results. There were no significant flow rate differences over a 3-year time period for unstimulated and stimulated parotid and submandibular/sublingual flow rates.

Conclusions. Major salivary gland output is age-stable in healthy persons over a 3-year period. The data from this study suggest that salivary gland dysfunction in an older person should not be considered a normal process of aging.

SALIVA plays a critical role in the maintenance of oral health. Salivary functions include the preservation, protection, and repair of oral mucosal tissues, remineralization of teeth, and the modulation of viral, fungal, and bacterial populations. The salivary fluids aid in food breakdown, bolus formation, and taste facilitation, and they can buffer acids from the external and internal environments (1). Alterations in salivary gland function can have deleterious effects on oral and systemic health (e.g., 1,2). Many elderly individuals complain of oral dryness, difficulty swallowing, diminished taste, and tooth loss. These complaints have been attributed, in part, to deteriorating oral defense mechanisms including salivary gland dysfunction.

Early physiological studies suggested that salivary gland dysfunction was a normal sequela of aging (e.g., 3). However, these studies were confounded by inclusion of subjects with overt medical problems. In the last two decades, there has been much interest in examining the role of aging on salivary physiology, and recent findings have led to a revision of these former conclusions.

There is a consensus that parotid function is stable across the age spectrum. Results of cross-sectional (4–16) and longitudinal (17,18) studies examining healthy individuals indicate that parotid salivary gland function is generally age-independent. Conversely, for submandibular/sublingual function, there is no consensus. Only two cross-sectional studies have examined submandibular/sublingual salivary flow rates in healthy individuals, and the results are conflicting. Pederson et al. (19) found an age-associated decrease in submandibular flow rates, while Tylenda et al. (12) found no changes in output across the human life span. To date, there are no published longitudinal submandibular/sublingual studies. For whole salivary flow rates and constituents, there are several reports of age-stable function (8,9,20–23), while other studies suggest declining function with increased age (3,9,21,23–25). Finally, several investigations have examined the output from the minor salivary glands. Two studies indicate that the function of these glands is age-independent (13,26) whereas two reports indicate age-related diminished function (8,14).

In summary, while there are conflicting data from numerous studies, it appears that salivary gland function does not undergo dramatic changes with increased aging in healthy persons. Nevertheless, to date there have been no longitudinal studies examining both parotid and submandibular/sublingual salivary flow rates in healthy individuals. Therefore, the purpose of this study was to examine unstimulated and stimulated major salivary gland flow rates in unmedicated, essentially healthy subjects, over a 3-year period.

METHODS

Subjects. — Individuals evaluated in this study included 37 persons between 26 and 90 years of age. The age and gender distribution of the subjects is given in Table 1. Subjects were volunteer participants in a normative aging program conducted by the National Institute on Aging at the Clinical Center of the National Institutes of Health, Be...
the subjects were healthy, community-dwelling Caucasians of middle socioeconomic status. None was treated for any systemic disease nor was taking any medication(s) for the duration of the study. Furthermore, all underwent rigorous medical, neurological, and laboratory screenings (27) to eliminate individuals with underlying medical disorders.

Collection of saliva. — All participants were seen by one investigator (JAS) at their first and second visits. The interval between examinations was approximately three years (36 ± 1.5 months, mean ± SD). All subjects refrained from eating, drinking, smoking, and oral hygiene for a minimum of 90 minutes prior to saliva collection, and were seen between 8:30 and 11 a.m. to control for circadian variances in salivary secretions (28). Unstimulated (resting) samples were collected initially for 5 minutes. For any subject displaying no unstimulated parotid saliva production after 5 minutes, a retest was performed. Only after two negative unstimulated test results, plus positive evidence of a stimulated secretion, was a subject considered to have an unstimulated flow rate of zero. This was followed by stimulation with 2% citrate applied to the dorsolateral surfaces of the tongue for 5 seconds at 30-second intervals (12). After a 2-minute equilibration period, stimulated secretions were collected for 2 minutes. Unstimulated and stimulated parotid saliva samples were collected from a single salivary gland with the use of a modified Carlson-Crittenden cup as described previously (4,7). Submandibular/sublingual saliva was collected from the orifice of Wharton’s duct with a micropipette attached to light suction as described previously (2). After collection, the volumes of all salivas were determined gravimetrically assuming a specific gravity of 1.0. Submandibular/sublingual saliva as defined in this study represents a combined submandibular/sublingual secretion due to the frequent common exit of the gland ducts (29).

Statistical analyses. — Intraclass correlation coefficients for unstimulated submandibular flow rate (0.978), stimulated submandibular flow rate (0.984), unstimulated parotid flow rate (0.855), and stimulated parotid flow rate (0.953) were calculated on nine healthy subjects. Differences between mean flow rates from Visit 1 to Visit 2 were evaluated by use of a Student’s paired t-test. The effect of gender on salivary function was tested at each visit and between visits. A Student’s t-test was used when mean values had a normal distribution, and a Mann-Whitney U procedure was used for nonparametric values. Regression analyses were performed on the changes in flow rates over the 3-year span to determine if there were any relationships to age at Visit 1 or gender. Data were analyzed with the use of RS1 software (BBN Software Products, Cambridge, MA). A criterion of \( p < .05 \) was accepted for significance in all statistical tests.

RESULTS

There were no gender-related differences in unstimulated and stimulated parotid and submandibular flow rates at Visit 1, Visit 2, for changes in flows over the 3-year span, and in the regression analyses. Thereafter, all analyses were performed with males and females combined. There were no significant changes in mean flow rates from Visit 1 to Visit 2 for unstimulated parotid and unstimulated and stimulated submandibular flow rates (Table 2). However, stimulated parotid flow rates increased significantly from Visit 1 to Visit 2 (Student’s paired t-test, \( p < .04 \), Table 2).

A subsequent analysis was performed comparing unstimulated and stimulated parotid and submandibular flow rates from Visit 1 to Visit 2 to determine if any changes were dependent upon age group. Overall, there were no significant changes over the 3-year period for all of the four flow rates in the three age groups with two exceptions. Stimulated parotid flow rates increased from Visit 1 (0.441 ± .052; mean ± SEM) to Visit 2 (0.581 ± .059) in the 14 individuals aged 40–59 years at Visit 1 (Student’s paired t-test, \( p = .0001 \)). Unstimulated submandibular flow rates increased slightly (Student’s paired t-test, \( p = .05 \)) from Visit 1 (1.012 ± .017) to Visit 2 (1.042 ± .018) in the 16 individuals aged 60 + years at Visit 1.

Flow rate differences over the 3-year time period for unstimulated (Figure 1, top panel) and 2% citrate-stimulated (Figure 1, bottom panel) parotid saliva revealed no significant age-related trends across the age range studied. The longitudinal results of unstimulated (Figure 2, top panel) and 2% citrate-stimulated (Figure 2, bottom panel) submandibular gland saliva also indicate no significant age-related trends.

DISCUSSION

The results of this study demonstrate, in general, that unstimulated and stimulated parotid and submandibular salivary gland flow rates do not change over 3 years in different-aged, healthy males and females. The parotid gland findings corroborate findings from cross-sectional and longitudinal studies which examined output (4,5,7-9,12-17) and constituents (5,6,10,11,18).

The longitudinal submandibular results in this study are consistent with one cross-sectional study (12) using identical salivary collection techniques. They also corroborate find-
Figure 1. Unstimulated (top panel) and 2% stimulated (bottom panel) parotid salivary flow rate differences over a 3-year span among 37 generally healthy people aged 26–90 years at initial visit. Males (n = 18) are designated by X, females (n = 19) are designated by O. Linear regression analysis for unstimulated parotid flow rates yields $r^2 = .01$ ($p > .05$) and for stimulated parotid flow yields $r^2 = .001$ ($p > .05$).

Figure 2. Unstimulated (top panel) and 2% stimulated (bottom panel) submandibular salivary flow rate differences over a 3-year span among 37 generally healthy people aged 26–90 years at initial visit. Males (n = 18) are designated by X, females (n = 19) are designated by O. Linear regression analysis for unstimulated submandibular flow rates yields $r^2 = .003$ ($p > .05$) and for stimulated submandibular flow yields $r^2 = .019$ ($p > .05$).

Findings from a recent investigation which utilized identical collection techniques with a stronger stimulus (10% citric acid), and reported that submandibular flow rates were not different between young (age 29–40 years) and old (age 60–97 years) healthy persons (30). These findings contrast with one study (19) which demonstrated decreased resting and post-stimulation submandibular flow rates in an older population using a different collection technique. However, older individuals in this study experienced a greater increase from resting to post-stimulation flow rates (792%) compared to younger individuals (455%) (19), suggesting that older persons were at least as capable of responding to a salivary stimulus compared to younger persons. In this study, the average post-stimulation flow rate of the elderly group (equivalent to 8 minutes following the initiation of lemon drop stimulation and 5 minutes following the completion of stimulation) was approximately 72% that of the younger group (19). While Wu et al. (30) reported no age-related flow rate differences 4 minutes after the initiation of stimulation, average flow rates for the older individuals were ap-
approximately 55% of the younger group 20 and 30 minutes after the initiation of stimulation. However, flow rates in both groups did not diminish over time: stimulated submandibular flow rates in the young group increased over the 30-minute time period (slope = .007, p > .05) while they were essentially stable over time in the older group (slope = -.001, p > .05) (30). Therefore, it appears that older individuals are able to respond immediately to a gustatory stimulus as well as young individuals, and maintain function for an extended period of time.

The most common design in gerontological studies is cross-sectional, comparing data from subjects of different ages at a single point in time (31). This design has certain weaknesses in identifying a true aging effect. The results, for example, may reflect a cohort effect. A longitudinal analysis of a population avoids this limitation of a cross-sectional study by holding the cohort effect constant. If cross-sectional and longitudinal findings are in the same direction (either increasing, decreasing, or stable), then a true aging effect has been demonstrated (31). Therefore, with the exception of the Pederson et al. (19) study, results from cross-sectional (12,30) and longitudinal investigations (present study) are consistent and suggest that submandibular salivary function is age-stable in healthy persons.

The findings in this study that unstimulated parotid and submandibular flow rates were stable over a 3-year period and not associated with age are important, since it is these secretions which play a vital role in maintaining oral health (e.g., 1,2). Alterations in these unstimulated fluids can result in deleterious consequences to an individual’s oral and systemic health since they confer protection to the host throughout the day and night. Stimulated secretions were also age-independent in this study. This is an additional critical finding, since stimulated fluids reflect the functional capacity of the salivary gland, and play a major role during meal time for mastication and deglutition. A diminished functional capacity could cause altered chewing, changes in nutritional intake, dysphagia, or predispose a person to aspiration pneumonia.

In contrast to the functional studies previously mentioned, histomorphometric investigations of major salivary glands have shown an age-related decrease in the proportion of remaining acinar tissues (e.g., 32,33). Acinar cells are considered to be the only site of water secretion in the salivary gland (34), and a decrease in the number of acinar cells would be predicted to result in a decrease in salivary secretion. In addition, an age-related decrease in the computed tomographic numbers of major salivary glands has been reported (35,36). However, Ariji et al. (36) found that the decrease in quantitative computed tomographic numbers of submandibular glands in individuals younger than age 40 years (r = -.40) was considerably greater than the decrease in individuals aged 40+ years (r = -.29) (36). Scott et al. (33) proposed the secretory reserve hypothesis to explain the discrepancy in findings between functional and histomorphometric studies. This hypothesis suggests that younger persons may possess an excess of acinar cells beyond that required for “normal” function. As age increases, it is postulated that this reserve is diminished and replaced by nonsecretory components such as adipose or connective tissue. As a result, older people may lose their hypothesized secretory reserve, but retain an adequate quantity of acinar cells to maintain physiologic secretory abilities. Following from this hypothesis, an elderly individual would not easily secrete fluid amounts beyond that which is required for “normal” function. Studies have begun to critically test this hypothesis. The parotid gland can sustain a high stimulated secretory ability for an extended period of time in both young and old persons (30). Extended stimulated submandibular flow rates increase over time in young individuals and remain stable in older individuals, demonstrating an age-related difference (30).

There are several limitations to this study. The length of the study was only 3 years, considerably shorter than the 10-year span in two previous parotid function studies (17,18). In addition, the number of study participants was small. This may partially account for the significant increase in stimulated parotid saliva over the 3-year time period (Table 2), yet this result was evident only in the group aged 40–59 years. Despite the small sample size, there were no observable decrements over the 3-year period for any of the four flow rates across the human life span. Larger and longer investigations utilizing individuals from different socioeconomic and racial/cultural backgrounds are clearly indicated.

The data from this study have clinical ramifications. Complaints of a dry mouth and salivary gland dysfunction in an older person should not be considered a normal process of aging. They are probably the result of systemic diseases and their treatments, including numerous medications (e.g., 37). Rather, the cause of the salivary gland dysfunction should be carefully evaluated. The dental profession can use convenient methods (38) to monitor secretory function over time as a component of routine clinical examinations. Once salivary gland hypofunction has been detected, clinical procedures and therapies can be initiated to combat the deleterious consequences of diminished function.

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