**INTRODUCTION**

Recent systematic literature research has shown that older people run a high risk of oral problems such as orofacial pain and loss of natural teeth. A possible explanation could be that the cognitive and motor impairments resulting from dementia cause a decrease in self-care and as such, a worsening of oral health. An alternative explanation is that cognition and oral health influence each other. Animal studies show that a decrease in masticatory activity, for example, due to a soft diet or loss of teeth, causes memory loss and neuronal degeneration. The relationship between mastication and cognition has also been researched in human studies, but a cause-effect relationship has not been proven. It is likely that multiple factors play a role in this relationship, such as self-care, nutrition, stress and pain.
between mastication and cognition, with a focus on older people with dementia.

2 | ANIMAL RESEARCH

A longitudinal study of mice examined the effect of food hardness on spatial memory and learning ability. A first group of animals was given hard food pellets; a second group was first given hard food, and then powdered food; and a third, "rehabilitated" group was first given hard food, then powdered food and finally hard food again. The experiment was carried out on adult and aged animals, and under two different sets of conditions: an "impoverished environment" (a standard plastic cage) and an "enriched environment" (a larger cage containing a variety of toys). At the end of each experiment, the animals' spatial learning ability was tested by means of a water maze. The results of this experiment were interesting: under impoverished conditions, ageing itself led to poorer performance. A soft diet also led to poorer performance, both in adult and in aged mice. An enriched environment had a positive influence on performance: adult mice from the enriched environment performed better than the comparable control group from the standard environment.

In the adult (but not the aged) group, rehabilitation with hard food led to improved performance, irrespective of the living environment. The older, rehabilitated mice recovered to normal performance. In the adult group, rehabilitation with hard food led to improved performance, irrespective of the living environment. The older, rehabilitated mice recovered to normal performance levels only if they lived in the enriched environment; rehabilitated aged animals living in the standard environment did not display this recovery.

Comparable results were seen in another study. In aged mice, molars in the upper jaw were extracted and the mice were kept for 3 weeks in either "standard" or "enriched environment" cages. The behavioural effects of these actions were then assessed using a water maze. The proliferation and differentiation of newborn neurons were assessed post-mortem, along with the development and retention of existing neurons. Molar loss turned out to have a negative influence on brain function: molarless mice displayed poorer spatial memory and learning ability. This group also developed fewer new neurons and retained fewer existing neurons than did fully dentate mice. An enriched environment had a positive influence: mice from the enriched environment had better spatial memory, greater learning ability, more newborn neuron proliferation and greater neuron retention than the mice from the standard environment. There was also a significant interaction effect from the two factors of "environment" and "molar loss" with regard to the survival of existing neurons: a molarless mouse in the standard environment retained fewer neurons than did a molarless mouse in the enriched environment, and no <25% fewer than a mouse in the enriched environment that had retained its teeth. In the enriched environment, a molarless mouse did not, incidentally, show significantly different scores than a fully dentate mouse. The nature of the environment therefore appeared to cancel out the negative effect of molar extraction in this study.

In 2016, an animal study showed that the effect of an enriched environment in preventing Alzheimer's disease in mice arose principally through the degree of physical activity and that solitary running in a wheel had the same protective effect as living in an enriched environment. Mastication could be regarded as a form of physical activity, one which also stimulates cerebral blood flow. In many cases, the restoration of masticatory activity is not brought about simply by a modification of diet; dental intervention is often required to restore masticatory ability. This matter was examined in an animal study in which the crowns of the upper molars were artificially abraded in a group of aged mice. A water maze was then employed to determine the behavioural effects of this intervention, and neural plasticity (ie, responsive adaptations in the organisation of cell structures in the brain) was established post mortem. The mice all lived in "standard" conditions. The results showed that molar abrasion was linked to poorer spatial memory and reduced neural plasticity, especially in the hippocampus, compared to the control group. It also became clear that the longer the mouse had abraded molars, the more prominent this worsening became. A number of mice were given a new molar crown after 10 days. The restored masticatory function resulted in improved learning ability and neural plasticity, although not to the levels of mice that had retained their original molars. In mice whose molars were restored in this way, spatial memory improved up to a level of 74% of the control group of mice who had retained their own teeth. Compared with the group that had not received crowns, this was an improvement of 150%. An unfortunate shortcoming of this study is that it measured only the effect of reduced masticatory ability, without regard to the possible presence and role of pain during the intervention.

3 | HUMAN RESEARCH

Although animal studies are extremely interesting and can indicate directions for follow-up research, their findings cannot simply be extrapolated to the human population. For this reason, studies of human subjects are needed, and this necessitates a different approach. A number of studies on the effects of mastication on cognition have been carried out in healthy adults. Patient studies have also been done, for instance, with older persons with dementia.

3.1 | Mastication and cognition in cognitively intact adults

Research studies of human subjects have shown that chewing of a piece of gum has an acute and positive effect on working memory. Even mood might be positively influenced by chewing gum: in a small study, it was found that mildly depressed patients who received medicinal treatment benefitted from complementary (sugar-free, flavourless) chewing gum therapy to relieve somatic symptoms of depression such as appetite loss. Although these are interesting and encouraging results, some studies have failed to replicate them, and others have even found negative effects of gum chewing on cognitive performance measures. Moreover,
this kind of research is often performed only on young adult sub-
jects even though age-dependent differences have been found in
the response to mastication, for instance, in cerebral blood flow. The
fact that excessive gum chewing can lead to pain and fatigue
in the jaw muscles means that some restraint should always be
exercised when recommending gum chewing. Potentially, posi-
tive long-term effects of gum chewing have not been adequately
demonstrated.

A large-scale Swedish population study of older community-
dwelling people (n = 557, aged 77 or older) showed that respon-
dents whose cognitive function screening test score indicated the
possible onset of dementia also had more difficulty chewing hard
food such as apples. The number of natural (as opposed to pro-
thetic) dental elements had no influence on this outcome. The au-
thors concluded that tooth loss did not necessarily lead to cognitive
impairment as long as there were no masticatory difficulties. The
relationship between cognitive function and masticatory ability has
also been studied in a population of older, cognitively intact, inde-
dependently living Dutch persons wearing full dental prostheses.
Cognitive function was measured using a neuropsychological test
battery. Masticatory function was assessed by measuring maxi-
mum mouth opening, maximum lateral and forward jaw movement,
maximum bite force and the number of occluding pairs. Complaints
about the stomatognathic system, with regard to orofacial pain and
headache, were assessed using the Axis-II questionnaire by the
Research Diagnostic Criteria for Temporomandibular Disorders
(RDC/TMD). By combining the scores for various neuropsy-
chological tasks, an "episodic memory" domain and an "executive
function" domain were created. Executive function is an import-
ant concept within neuropsychology and describes goal-directed
behaviour, including working memory, inhibition, planning and
attention. The prefrontal cortex is particularly strongly associ-
ated with executive function, although other sub-cortical areas
and networks in the brain are also involved in executive function.
The Dutch study revealed that among full dental prosthesis wear-
ers, performance in executive function was poorer when there
were also complaints about masticatory function. Performance
in episodic memory was positively associated with bite strength.
Backward multiple regression analysis was then employed in order
to analyse the influence of the different variables involved. This
showed that 19% of episodic memory function could be predicted
by jaw mobility and bite strength and that 22% of performance
variation in executive function was related to complaints about
masticatory function.

Another study used imaging techniques to map the effects of
mastication on cerebral blood flow and revealed that the frontal
cortex, in particular, became more active during mastication. The
effect of mastication on the activation of these areas was stronger
in older individuals. It could therefore be the case that mastication
stimulates cerebral blood flow, particularly in the frontal cortex,
which could then have an influence on executive function and there-
fore on cognitive performance. In a small clinical study (n = 9) of
middle-aged test subjects with unilateral loss of the first and second
inferior molars, the electromyographic (EMG) activity of the left
and right masseter muscles was measured during a clench task, and
pupil diameters were measured both at rest and during a sensory
search task. Pupil diameter increases in reaction to cognitive tasks
requiring memory and attention (mydriasis), a phenomenon which
is used as an indicator of mental arousal in psychophysiological ex-
periments. A digit retrieval task was also given, in which as many
numbers as possible had to be identified on a 10 × 10 matrix of digits
during 30 seconds. Participants were fitted with dental implants,
and then, three different situations were studied: mouth open, with-
out crowns on the implants; mouth closed, without crowns on the
implants; and mouth closed, with crowns on the implants. During the
digit retrieval task, all participants displayed asymmetry both in EMG
activity and in pupil diameter (anisocoria). The placement of implants
restored dental occlusion, and both asymmetric EMG activity and
the anisocoria disappeared. The second situation (mouth closed,
no crown) yielded the poorest intellectual performance, and the
third situation (mouth closed, with crowns) yielded the best intellec-
tual performance. The restoration of occlusion seemed to contribute
towards the restoration of cognitive function. Pupil diameter asym-
metry however remained, to a smaller degree, as long as 6 months
after crowns had been fitted to the implants. A possible explanation
for this might be that sensory asymmetry resulting from the loss of
input from periodontal mechanoreceptors was not, or not entirely,
removed by treatment with implants.

3.2 Mastication and cognition in older people
with dementia

The relationship between oral health, masticatory function and cog-
nitive function has also been studied in older people with demen-
tia. In a group of 60 community-dwelling persons, the oral health
of Alzheimer’s disease (AD) patients with mild, moderate or serious
cognitive impairment was compared with the oral health of a control
group. Subjective oral health was determined using the Geriatric
Oral Health Assessment Index (GOHAI) questionnaire; a higher
GOHAI score implies a more positive perception by the respondent
of their oral health. Objective oral health was determined by oral
examination, which looked at the presence and condition of natural
and prosthetic dental elements. The Decayed-Missing-Filled Teeth
(DMFT) index was determined, and the presence of plaque and tar-
tar was assessed. The GOHAI scores of all groups were comparable.
This is remarkable, because the AD group had poorer objective oral
health; they had fewer natural teeth and a higher DMFT score, and
this group was more likely to suffer from an oral health disorder.
The AD group with serious cognitive impairment had the highest
GOHAI scores, that is, had the most positive perception of their own
oral health. In answering the GOHAI questions, study participants
with AD were assisted by their caregivers. The authors concluded
that, in terms of their own subjective perception, participants with
and without AD were positive about their own oral health, but that
those participants with AD actually showed oral health problems
that increased with their level of cognitive impairment. This shows
that neither these participants nor their caregivers were particularly skilled at assessing oral health.\textsuperscript{26}

In another study, the masticatory function (amongst other variables) of 29 older people with dementia was compared with that of 22 cognitively healthy matched subjects.\textsuperscript{27} Masticatory function was measured as the ability to mix a two-coloured chewing gum. The number of natural and prosthetic dental elements was similar in both groups. The persons with dementia turned out to have three times as much visible plaque, to be more dependent on others in the execution of daily life activities and to be more frequently undernourished than the control group. They also performed less well at the two-colour gum-mixing task. The authors concluded that masticatory function appeared to be more closely related to cognitive impairment than to the number of dental elements. The loss of masticatory ability was explained by a reduction in motor skills resulting from dementia.\textsuperscript{27} In a group of 114 older persons with dementia who were living in a nursing home or who regularly visited a day centre, masticatory ability was also measured using the two-colour gum-mixing approach. Their cognitive function was measured using a comprehensive neuropsychological test battery.\textsuperscript{28} Of the eight neuropsychological tests that were carried out, two turned out to have a significant relationship with masticatory function, namely "general cognition" and "word fluency".\textsuperscript{28} In a word fluency test, the participant was asked—in the course of a protocol-directed interview—to name as many words as possible within a certain category, within a certain short period of time. This task appeals to memory, planning and inhibition, and is therefore a good indicator of executive function. Only half of the 114 participants performed the two-colour chewing gum task. The most common reason for nonparticipation was concern among care staff about the possible agitation of the

\textbf{FIGURE 1} Interactions between mastication, cognition, stress and pain. Mastication has a regulatory effect on stress and also has positive effects on cognition and pain perception.\textsuperscript{12} In animals, reduced masticatory activity is linked to cognitive decline.\textsuperscript{5} Excessive mastication, however, can also cause pain.\textsuperscript{17} Pain causes stress\textsuperscript{32} and has a negative influence on masticatory activity,\textsuperscript{33} and on cognition.\textsuperscript{34} Cognitive changes such as dementia can both alter pain perception and limit pain communication.\textsuperscript{33} Cognitive decline can also have a negative effect on oral health.\textsuperscript{35} Research has not yet clearly revealed the nature of the influence that cognition may have on stress.\textsuperscript{35} Stress can lead to bruxism and/or oral parafunction\textsuperscript{12} and can also heighten sensitivity to pain (hyperalgesia).\textsuperscript{36} Although short-term stress has a performance-heightening effect, chronic stress has a negative effect on cognition\textsuperscript{12}
participants. Of the 58 participants who performed the two-colour gum-mixing task, 56 also completed the general cognition task and 51 completed the word fluency task. Correlations were investigated within these subgroups and it turned out that those participants who performed better at the gum-mixing task also displayed better cognitive performance, as shown by the general cognition test and the word fluency test.

4 UNDERLYING MECHANISMS

A variety of underlying mechanisms can be put forward to explain the relationship between masticatory ability and cognitive function. It is possible, for instance, that effective mastication of food leads to improved nutrition and that this contributes towards preservation of cognition. Another hypothesis is that mastication raises cerebral arousal levels, or that, as a physical activity, it contributes towards an enriched environment. It is also possible that active mastication contributes towards the reduction in stress and/or pain; for instance, an animal study found that gnawing and chewing during a stressful situation kept cognitive scores at the same level as they were in nonstressed control animals, while a stressed group that was prevented from gnawing and chewing showed significantly lower cognitive scores than the control group. It is also known that stress, whether or not caused by pain, has a negative influence on cognition. Figure 1 drafts a possible interaction model linking mastication, cognition, stress and pain.

5 CONCLUSION AND DISCUSSION

It could be plausible that a reciprocal relationship between mastication and cognition exists, as animal studies suggest, however, this relationship has not been sufficiently studied in human populations. It is probable that several factors play a role in this relationship, including self-care, motor function, nutrition, and stress and pain. A possible causal relationship between mastication and cognition is naturally of interest to anyone wanting to retain their cognitive strength, but it is perhaps of greatest importance to the group of vulnerable older people with dementia. It is therefore of great concern that oral health is particularly poor in this group.

When considering functional recovery in older people with dementia, account must of course be taken of the feasibility and patient burden of treatment and the possibility of a reduced acceptance of prosthetics. Treatment interventions in this group should concentrate on prevention, comfort, dignity and pain control.

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