4 N F M M B O E 5 B T U F % Z–× ¦ ð @ P Đ ©f ` J0M E V à J0

Keywords: Smell and taste dysfunction; Neurodegenerative and neuropsychiatric diseases

Introduction

Smell is one of the oldest senses in evolution, plays a key role in development, relationships, pleasure, health, safety and survival [1]. Smell is associated with memories, moods and emotions, food preferences, pheromones, mating and parent-infant bonding. Although humans are less dependent on smell for survival than other mammals, smell is critical for detecting polluted air and water, smoke and leaking gas, and spoiled foods [2]. Despite these important functions, smell has been one of the neglected senses.

Although the sense of smell functions as early as the fetal stage,decreased olfactory function occurs with aging, with over half of those between the ages of 65 and 80 and over three quarters of those over the age of 80 experiencing this problem [3]. In a sample with olfactory disorder, 68% of the patients presented with hyposmia and 32% with anosmia [4]. Olfaction has been notably worse in men in most studies [2,5] ,although there are some exceptions[6]. In the latter study, lower olfaction scores were also related to lower educational status.

An inability to identify smells or tastes predates the clinical symptoms of several neurodegenerative and neuropsychiatric diseases, highlighting their importance as markers for early interventions. Neurodegenerative diseases that have been associated with inferior smell identi cation include Parkinson's [7-12], Alzheimer's [9, 13,14] and a myotrophic lateral sclerosis [8] and the neuropsychiatric/smell disorder conditions include ADHD [15,16], anxiety disorders [17], Autism Spectrum Disorder [18-20], depression [21], eating disorders [22] and schizophrenia [23-26].

Most of the empirical studies have compared clinical and non-clinical groups on smell tests, although more recently, some longitudinal studies have documented sensory dysfunction in at-risk, rst degree relatives who later show the cardinal motor signs [8,27]. e University of Pennsylvania Smell Identi cation Test (UPSIT) is the most frequently used test [8], although several other shorter and less expensive versions have been developed including the Sni n Sticker Test (SST) [9], the Brief Smell Identi cation Test (B-SIT) [28], the Odor Stick Identi cation Test (OSIT) [8], the San Diego Odor Identi cation Test (SDOIT) [28] and most recently the peanut butter smell test [14]. ese tests, for example the Sni n' Sticks test has been signi cantly correlated with a visual analogue scale in at least one study [29].

e etiology and development of these sensory dysfunctions are not known, but the dopamine, norepinephrine, serotonin, acetylcholine and orbitofrontal cortex systems have been implicated in several of the neurodegenerative and neuropsychiatric conditions associated with smell dysfunction [8,38]. ese include, for examples, Parkinson's and ADHD. Although sensory tests have been developed for infants and young children who are noted to have hypo or hypersensitivity as well as sensory integration problems [33], longitudinal studies have not

Citation:) L H Ø G

of apathy relative to non-AD participants, but odor identi cation de cits were correlated with apathy levels, not depression, across the AD and non-AD samples [13].

Amyotrophic lateral sclerosis

In a study on amyotrophic lateral sclerosis (ALS) also known as Lou Gehrig's disease ALS patients' UPSIT scores were signi cantly lower than they were for a control group [72].

Sensory dysfunction in neuropsychiatric diseases

Sensory dysfunction is also an early marker for neuropsychiatric diseases including autism spectrum disorder, attention de cit/hyperactivity disorder, eating disorders, depression, obsessive compulsive disorder, posttraumatic stress disorder and schizophrenia, with the lion's share of the published research being on attention de cit/hyperactivity disorder and schizophrenia. And, as in neurodegenerative diseases, smell testing has beys/cP.

Citation:) L H Ø G

Limitations of e Literature and Future Directions

Odor identi cation de cits have been documented in many studies

*KDQL]DGHK $ %DKUDQL 0 0LUL 5 6DKUDLDQ $ 6PHOO LGHQWL¿FDWLRQ IXQFWLRQ LQ FKLOGUHQ ZLWK DWWHQWLRQ GH¿FLW K\SHUDFWLYLW\ GLVRUGHU 3V\FKLDWU\ ,QYHVWLJ

6FKHFNOPDQQ 0 6FKZHQFN & 7DXULQHV 5 •3•>`00 à@ Pð0 DQG 1H• 5´Pð05´Pð0pÀcpP0 ¼@ 5´Pð0

€b@ F D P0 À Ð 0 @ € 0 @ € `

%RKQHQ 1, 6WXGHQVNL 6$ &RQVWDQWLQH *0 0RRUH 5< 'LDJQRVWLF SHUIRUPDQFH RI FOLQLFDO PRWRU DQG QRQ PRWRU WHVWV RI 3DUNLQVRQ GLVHDVH D PDWFKHG FDVH FRQWURO VWXG\ (XU - 1HXURO

6WHUQ 0% 'RW\ 5/ 'RWWL 0 &RUFRUDQ 3 &UDZIRUG ' HW DO 2OIDFWRU\ IXQFWLRQ LQ 3DUNLQVRQ¶V GLVHDVH VXEW\SHV 1HXURORJ\

+DHKQHU $ +XPPHO 7 +XPPHO & 6RPPHU 8 -XQJKDQQV 6 HW DO 2OIDFWRU\ ORVV PD\ EH D ¿UVW VLJQ RI LGLRSDWKLF 3DUNLQVRQ¶V GLVHDVH 0RY 'LVRUG

.LP +- -HRQ %6 /HH -< &KR <- +RQJ .6 HW DO 7DVWH IXQFWLRQ LQ SDWLHQWV ZLWK 3DUNLQVRQ GLVHDVH - 1HXURO

.HUWHOJH / %UXJJHPDQQ 1 6FKPLGW $ 7DGLF 9 :LVVH & HW DO ,PSDLUHG 6HQVH RI 6PHOO DQG &RORU 'LVFULPLQDWLRQ LQ 0RQRJHQLF DQG ,GLRSDWKLF 3DUNLQVRQ¶V 'LVHDVH 0RYHPHQW 'LVRUGHUV

+DUD 7 +LUD\DPD 0 0L]XWDQL < +DPD 7 +RUL 1 HW DO ,PSDLUHG SDLQ SURFHVVLQJ LQ 3DUNLQVRQ¶V GLVHDVH DQG LWV UHODWLYH DVVRFLDWLRQ ZLWK WKH VHQVH RI VPHOO 3DUNLQVRQLVP 5HODW'LVRUG

0•OOHU $ 0•QJHUVGRUI 0 5HLFKPDQQ + 6WUHKOH * +XPPHO 7 2OIDFWRU\ IXQFWLRQ LQ 3DUNLQVRQLDQ V\QGURPHV - &OLQ1HXURVFL

0HVKRODP 5, 0REHUJ 3- 0DKU 51 'RW\ 5/ 2OIDFWLRQ LQ QHXURGHJHQHUDWLYH GLVHDVH D PHWD DQDO\VLV RI ROIDFWRU\ IXQFWLRQLQJ LQ $O]KHLPHU¶V DQG 3DUNLQVRQ¶V GLVHDVHV $UFK 1HXURO

:LOVRQ 56 $UQROG 6(6FKQHLGHU -$ %R\OH 3$ %XFKPDQ $6 HW DO 2OIDFWRU\ LPSDLUPHQW LQ SUHV\PSWRPDWLF $O]KHLPHU¶V GLVHDVH $QQ 1 < $FDG 6FL

+DZNHV &+ 6KHSKDUG %& *HGGHV -) %RG\ *' 0DUWLQ -(2OIDFWRU\ GLVRUGHU LQ PRWRU QHXURQ GLVHDVH ([S 1HXURO

%HQQHWWR / .XVFKQHU (6 +\PDQ 6/ 2OIDFWLRQ DQG WDVWH SURFHVVLQJ LQ DXWLVP %LRO 3V\FKLDWU\

(VFDORQD $)LHOG 7 6LQJHU 6WUXQN 5 &XOOHQ & +DUWVKRUQ . %ULHI UHSRUW LPSURYHPHQWV LQ WKH EHKDYLRU RI FKLOGUHQ ZLWK DXWLVP IROORZLQJ PDVVDJH WKHUDS\ - $XWLVP 'HY 'LVRUG

.DUV])5 9DQFH $ $QGHUVRQ 9$ %UDQQ 3* :RRG 6- HW DO 2OIDFWRU\ LPSDLUPHQW LQ FKLOG DWWHQWLRQ GH¿FLW K\SHUDFWLYLW\ GLVRUGHU - &OLQ 3V\FKLDWU\

5RPDQRV 0 5HQQHU 7- 6FKHFNOPDQQ0 +XPPHO % 5RRV0 HW DO ,PSURYHG RGRU 6HQVLWLYLW\ LQ $WWHQWLRQ 'H¿FLW +\SHUDFWLYLW\ 'LVRUGHU %LRORJLFDO 3V\FKLDWU\

*QVOHU '$)XFHWROD 5 .UHQJHO 0 6WHWVRQ 6 =LPHULQJ 5 HW DO $UH WKHUH FRJQLWLYH VXEW\SHV LQ DGXOW DWWHQWLRQ GH¿FLW K\SHUDFWLYLW\ GLVRUGHU" - 1HUY 0HQW 'LV

0XUSK\ .5 %DUNOH\ 5$ %XVK 7 ([HFXWLYH IXQFWLRQLQJ DQG ROIDFWRU\ LGHQWL¿FDWLRQ LQ \RXQJ DGXOWV ZLWK DWWHQWLRQ GH¿FLW K\SHUDFWLYLW\ GLVRUGHU 1HXURSV\FKRORJ\

$WDQDVRYD % *UDX[- (+DJH : +RPPHW & &DPXV 9 HW DO 2OIDFWLRQ D SRWHQWLDO FRJQLWLYH PDUNHU RI SV\FKLDWULF GLVRUGHUV 1HXURVFL %LREHKDY 5HY

0F&DIIUH\ 5- 'XII . 6RORPRQ *6 2OIDFWRU\ G\VIXQFWLRQ GLVFULPLQDWHV SUREDEOH $O]KHLPHU¶V GHPHQWLD IURP PDMRU GHSUHVVLRQ D FURVV YDOLGDWLRQ DQG H[WHQVLRQ - 1HXURSV\FKLDWU\ &OLQ1HXURVFL

)LHOG 7 'LHJR 0 +HUQDQGH] 5HOI 0)LJXHLUHGR % 6FKDQEHUJ 6 HW DO 6OHHS GLVWXUEDQFHV LQ GHSUHVVHG SUHJQDQW ZRPHQ DQG WKHLU QHZERUQV ,QIDQW %HKDY 'HY

0REHUJ 3- $JULQ 5 *XU 5(*XU 5& 7XUHWVN\ %, HW DO 2OIDFWRU\ G\VIXQFWLRQ LQ VFKL]RSKUHQLD D TXDOLWDWLYH DQG TXDQWLWDWLYH UHYLHZ 1HXURSV\FKRSKDUPDFRORJ\

1DND $ 5LHGO 0 /XJHU $ +XPPHO 7 0XHOOHU &$ &OLQLFDO VLJQL¿FDQFH RI VPHOO DQG WDVWH GLVRUGHUV LQ SDWLHQWV ZLWK GLDEHWHV PHOOLWXV (XU $UFK 2WRUKLQRODU\QJRO

6WHLQEDFK 6 5HLQGO : 'HPSÀH $ 6FKXVWHU $:ROI 3 HW DO 6PHOO DQG WDVWH LQ LQÀDPPDWRU\ ERZHO GLVHDVH 3/R6 2QH H