Salivary biomarkers in childhood-onset obsessive compulsive disorder: Analyses of pro-inflammatory cytokines in a pilot cohort

Clara Westwell-Roper^{1,2}, Zainab Naqqash¹, Antony Au¹, Boyee Lin¹, Cynthia Lu¹, John R. Best¹, Li Shao⁴, Clare L. Beasley^{2,3,4*}, S. Evelyn Stewart^{1,2,3*}

¹Provincial OCD Program, BC Children's Hospital Research Institute; ²Department of Psychiatry, Faculty of Medicine, University of British Columbia;

³BC Mental Health and Substance Use Research Institute; ⁴Djavad Mowafaghian Centre for Brain Health; Vancouver, BC, Canada. *Co-Principal Investigators.

Introduction Clinical and epidemiological studies suggest an association between pediatric obsessive-compulsive disorder (OCD) and immune dysregulation, including mucosal inflammation. The objective of this pilot study was to determine the feasibility of measurement of salivary immune mediators in children and youth with OCD and healthy controls. Immune system (dys)function in OCD Increased risk for OCD after recurrent throat infections High prevalence of immune-related disorders Neuroimmune interactions Elevated peripheral pro-inflammatory cytokines Sympathetic outflow from brain Low plasma immunoglobulin A (IgA) Hypothalamic-pituitary-adrenal axis Microglial activation throughout neurocircuitry Blood-brain-barrier Enteric nervous system Myeloid cell differentiation/trafficking Non-specific factors Acute and chronic stress Early life adversity Systemic inflammation Comorbidities Oral health Salivary immune components Oral/mucosal Hygiene Pro-inflammatory cytokines inflammation Dental appliances Stress-responsive proteins Antibodies, antimicrobial peptides hysical comorbidities

Diet and activity

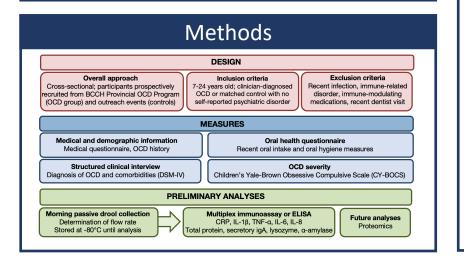


Table 1. Demographics and oral health of participants

Characteristic	Control, n=46	OCD, n=41	p ^a
Current age, mean ± SD	16.2 ± 1.1	13.0 ± 3.1	<0.001
Gender, % female of total	65	46	0.076
White/Caucasian, % of total	13	62	<0.001
Asian ^b , % of total	44	8	<0.001
Any flossing, % of total	85	41	<0.001
Reported good oral health, % of total	88	84	0.747
Braces or retainer, % of total	46	38	0.473
CY-BOCS score, mean ± SD	NA	22.0 ± 7.6	NA

^aAs determined by chi-squared (categorical variables) or Mann-Whitney U-test (continuous variables). ^bDefined as Chinese, Filipino, Japaneses, Korean, West Asian, Southeast Asian, South Asian, or Arab. Other self-identified groups based on race/ethnicity/ancestry each constituted <5% of participants.

Table 2. Multiple linear regression analyses of salivary proinflammatory cytokines and stress-responsive proteins

	IL-6		IL-1β		TNF-α		CRP	
Variance explained by model ^a	49.8 % (p=0.003)		40.0% (p=0.002)		26.5% (p=0.088)		14.2% (p=0.482)	
Variable	β	р	β	р	β	р	β	р
Age	-0.061	0.671	-0.089	0.444	-0.246	0.062	0.033	0.815
Female gender	0.172	0.182	0.200	0.087	0.178	0.158	-0.021	0.882
White/Caucasian	0.130	0.321	0.222	0.075	-0.152	0.262	0.067	0.651
Severe OCD ^b	0.274	0.034	0.258	0.029	0.257	0.047	0.076	0.580
Any flossing	0.173	0.195	0.115	0.346	0.016	0.904	-0.333	0.026
Braces	0.284	0.033	0.229	0.051	0.244	0.058	0.037	0.789
Good oral health	-0.471	<0.001	-0.258	0.023	-0.240	0.050	0.055	0.682
Total protein	0.082	0.529	0.209	0.070	0.216	0.089	0.232	0.090
Flow rate	0.291	0.023	0.340	0.004	0.172	0.170	0.271	0.045
BMI ^c	0.562	0.138	0.010	0.96	0.292	0.596	0.094	0.794

a Change in R-squared following initial adjustment for technical assay plate. Secretory IgA, pH, amylase, and Iysozyme were associated with total protein levels; secretory IgA was additionally predicted by self-reported good oral health (β=-0.381, p=0.004). Based on CY-BOCS score ≥24. Added to model in separate analyses for OCD group (BMI not collected for control group).

Summary

- Passive drool collection is feasible in children with OCD and allows for detection of multiple inflammatory markers.
- Severe OCD (rather than overall OCD status) and self-rated good oral health predicted salivary IL-6, IL-1β, and TNF-α in this preliminary cohort. There was no association with secretory IgA, pH, amylase, or lysozyme.

Conclusions

- Saliva may provide a minimally-invasive tool for assessing mucosal immunity and neuroendocrine-immune interactions in psychiatric disorders.
- Immune mediators present in saliva likely reflect both the systemic and local inflammatory environments.
- Symptom severity may be an important determinant of inflammation across multiple psychiatric disorders.

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Email: cwestwellroper@bcchr.ubc.ca Twitter: @cwestwellroper