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Communities advancing the studies of Tribal nations across their lifespan: Design, methods, and baseline of the CoASTAL cohort

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ABSTRACT

The CoASTAL cohort represents the first community cohort assembled to study a HAB-related illness. It is comprised of three Native American tribes in the Pacific NW for the purpose of studying the health impacts of chronic, low level domoic acid (DA) exposure through razor clam consumption. This cohort is at risk of DA toxicity by virtue of their geographic location (access to beaches with a history of elevated DA levels in razor clams) and the cultural and traditional significance of razor clams in their diet. In this prospective, longitudinal study, Wave 1 of the cohort was comprised of 678 members across the human lifespan, with both sexes represented within child, adult, and geriatric age groups. All participants were followed annually with standard measures of medical and social history; neuropsychological functions, psychological status, and dietary exposure. DA concentrations were measured at both public and reservation beaches where razor clams are acquired. Multiple metrics were piloted to further determine exposure. Baseline data indicated that all cognitive and psychological functions were within normal limits. In addition, there was considerable variability in razor clam exposure. Therefore, the CoASTAL cohort offers a unique opportunity to investigate the potential health effects of chronic, low level exposure to DA over time.

1. Introduction

The role that ocean waters play in global health is increasingly recognized as an important public health issue (Knap et al., 2002). The growing demand for fish and shellfish, coupled with widespread contamination and development in coastal areas, has challenged the fragile ecological balance that exists between land-dwelling and marine populations. Health concerns stemming from the ocean generally revolve around exposure to agents in the marine ecosystem such as environmental pollutants, metals, and biotoxins. Marine scientists have identified the phenomenon of harmful algal blooms (HABs) as an important source of marine biotoxins (Erdner et al., 2008). While microscopic algae are essential for ocean life, there are a few dozen species that produce powerful biotoxins. When these algae bloom in excess, there can be devastating health effects in seabirds, marine mammals, and humans. Harmful algal blooms have been linked to human death and illness, and mass killings of fish, marine mammals, and seabirds (Stommel and Watters, 2004). Oceanographic monitoring data suggest that there are more toxic algal species, frequency of HABs appears to be increasing, and toxic strains of algae are spreading across new geographical regions (Luckas et al., 2005).

There are five clinical poisoning syndromes associated with HABs, but only one, amnesic shellfish poisoning, has a well-defined neurologic, gastrointestinal, and neuropsychological syndrome characterized by profound memory disorder. Domoic acid (DA), the causative agent in amnesic shellfish poisoning, is produced by microscopic algae of the genus, *Pseudo-nitzschia* (Bates et al., 1989). The potential risk of DA to human health was discovered in 1987 on Prince Edward Island, Canada, where 153 cases of acute intoxication were documented (including 4 deaths) (Perl et al., 1990a,b; Teitelbaum, 1990; Teitelbaum et al., 1990). These clinical cases were linked to the consumption of DA-contaminated mussels

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harvested from the Cardigan River. Symptomology included nausea, vomiting, abdominal cramping, excessive respiratory secretions, coma, and death. Neurological symptoms such as headaches, hallucinations, confusion, and memory impairment were also reported in exposed individuals. Clinical evaluations of 14 adults after the outbreak revealed that 12 had severe antegrade memory deficits with relative preservation of higher cortical functions (Teitelbaum, 1990; Teitelbaum et al., 1990). Affected individuals had difficulty remembering events that had occurred after DA exposure. Subsequent to this incident, environmental sampling revealed blooms of *Pseudo-nitzschia* at the locations where the mussels had been harvested. This episode firmly established the serious and complex health effects associated with the oral ingestion of DA-contaminated shellfish.

In response to the Canadian episode of DA poisoning, scientific investigations of DA toxicity and neurotoxicity were initiated in the laboratory with animal models. The neurobehavioral signature of this compound has been detailed by Grant et al. (2010). DA acts as a strong emetic and is associated with adverse changes in both brain and behavior. The hippocampus is the primary site of injury in the central nervous system (CNS). The adverse consequences of DA exposure are not limited to a single behavioral effect, and treatment-related changes have been documented in motor, cognitive, and emotionality domains. Research has also demonstrated that functional losses can be persistent and injuries to the CNS can be progressive over time. Given that DA is an increasingly prevalent biotoxin in the world's oceans (Trainer et al., 2012), there is an urgent need to identify study populations that have documented (and measurable) low-dose, chronic exposures to DA. Ideally these populations can be assessed for evidence of clinical (and subclinical) exposure effects and can be followed longitudinally to evaluate changes across time. We report here the identification and initial characterization of such an exposure cohort, as well as details regarding the methodology of this study. Since a wide range of specialized methods are used to describe the cohort and measure cognition as well as exposure across the lifespan, baseline cohort results will immediately follow each category of measurement.

2. Methods and results

2.1. Study background and community involvement

The Communities Advancing the Studies of Tribal Nations Across the Lifespan (CoASTAL) cohort evolved from a community based, environmental health initiative of the Quileute Indian Nation in response to concerns about rising levels of DA in the Pacific Northwest, USA. Shellfish managers, Tribe Council members, and the Quileute Health Clinic participated in the design, implementation, and interpretation of a pilot study that raised the possibility of DA neurotoxicity among some people in their community. However, since exposure and cognition are both complex processes, further investigation with a larger sample over time was needed to clarify and extend the findings. Subsequently, neighboring Pacific coast Tribal Nations both north (Makah Tribe) and south (Quinault Indian Nation) joined the study team to further examine the potential health effects of low levels of DA exposure by razor clam consumption.

Using a community-based participatory model, the contributions of these Tribal Nations to the cohort study included assistance with research design and implementation, including recruitment, data collection, interpretation of results, and community outreach and education. This was facilitated through hiring local study coordinators (Tribal members) and assembling local data collection field teams, community advisory boards, and medical advisory groups. Tribal fisheries experts, shellfish researchers, and environmental health managers assisted with providing environmental, razor clam harvest and DA data, and critical linkages with Tribal Councils and other community leaders. Community events such as health fairs, elder dinners, and treaty celebrations were used as venues to introduce the study to the Tribal Nations and to distribute informational brochures about the study and educational materials about memory, DA and healthy diets. The CoASTAL cohort study was funded by the National Institute of Environmental Health Science and data collection began in the summer of 2005 in the areas depicted below in Fig. 1.

2.2. The CoASTAL cohort

2.2.1. Recruitment

This study represents the methodology and baseline data collection for Wave 1 (the first 5 years) of a prospective longitudinal cohort study of DA neurotoxicity in the Pacific Northwest. The cohort was comprised of 678 participants. Initially recruitment was limited to individuals in the following age groups: school age children (6–12 years), adults (18–64 years), and geriatric (65+ years). Sampling frames for each site were derived through tribal registries from the Quinault, Quileute, and Makah reservations. After sorting by age, potential participants were randomly selected based upon the total number of enrolled members for each study site. A letter of invitation was sent to each selected adult participant and to the parents or primary caregivers of child participants. The letter of invitation explained the nature, purpose, and general procedures of the study.

Field coordinators scheduled baseline visits for all study participants. If a participant declined participation, their name was removed from the list and an alternate was randomly selected within their age group. This sequence was continued until the goal recruitment numbers were met at each location or until the lists of potential participants were exhausted. An alternative methodology was used to recruit the infant sample as they were not included on the tribal enrollment registries. Flyers were posted in health clinics, on bulletin boards, and in local newspapers on each reservation asking parents/primary caregivers to volunteer their

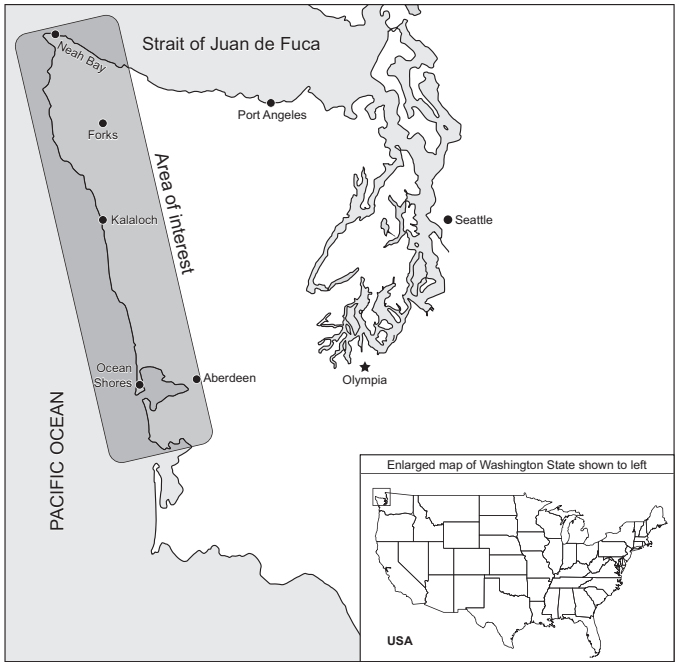

Fig. 1. Study region.